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PROVISIONAL APPLICATION COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION under 37 CFR 1.53 (c).

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TITLE OF THE INVENTION (280 characters)

CONSENSUS/ANCESTRAL IMMUNOGENS

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ENCLOSED APPLICATION PARTS *(check all that apply)*

☒	Specification	Number of Pages	94	☐ Applicant claims "small entity" status. ☐ "Small entity" statement attached.	
☒	Drawing(s)	Number of Sheets	123	☒ Other (specify)	ABSTRACT (1 page)

METHOD OF PAYMENT *(check one)*

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The invention was made by an agency of the United States Government or under a contact with an agency of the United States Government.

☐ No.

☐ Yes, the name of the U.S. Government agency and the Government contract number are:

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☐ Additional inventors are being named on separately numbered sheets attached hereto.

PROVISIONAL APPLICATION FILING ONLY

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SPECIFICATION

CONSENSUS/ANCESTRAL IMMUNOGENS

This application is related to Provisional Application No. 60/503,460, filed September 17, 2003, the entire content of which is incorporated herein by reference.

TECHNICAL FIELD

The present invention relates, in general, to an immunogen and, in particular, to an immunogen for inducing antibodies that neutralize a wide spectrum of HIV primary isolates and/or to an immunogen that induces a T cell immune response. The invention also relates to a method of inducing anti-HIV antibodies, and/or to a method of inducing a T cell immune response, using such an immunogen. The invention further relates to nucleic acid sequences encoding the present immunogens.

BACKGROUND

The high level of genetic variability of HIV-1 has presented a major hurdle for AIDS vaccine development. Genetic differences among HIV-1 groups M, N, and O are extensive, ranging from 30% to 50% in *gag* and *env* genes, respectively (Gurtler et al, J. Virol. 68:1581-1585 (1994), Vanden Haesevelde et al, J. Virol. 68:1586-1596 (1994), Simon et al, Nat. Med. 4:1032-1037 (1998), Kuiken et al, Human retroviruses and AIDS 2000: a compilation and

analysis of nucleic acid and amino acid sequences (Theoretical Biology and Biophysics Group, Los Alamos National Laboratory, Los Alamos, New Mexico)). Viruses within group M are further classified into nine genetically distinct subtypes (A-D, F-H, J and K) (Kuiken et al, Human retroviruses and AIDS 2000: a compilation and analysis of nucleic acid and amino acid sequences (Theoretical Biology and Biophysics Group, Los Alamos National Laboratory, Los Alamos, New Mexico, Robertson et al, Science 288:55-56 (2000), Robertson et al, Human retroviruses and AIDS 1999: a compilation and analysis of nucleic acid and amino acid sequences, eds. Kuiken et al (Theoretical Biology and Biophysics Group, Los Alamos National Laboratory, Los Alamos, New Mexico), pp. 492-505 (2000)). With the genetic variation as high as 30% in *env* genes among HIV-1 subtypes, it has been difficult to consistently elicit cross-subtype T and B cell immune responses against all HIV-1 subtypes. HIV-1 also frequently recombines among different subtypes to create circulating recombinant forms (CRFs) (Robertson et al, Science 288:55-56 (2000), Robertson et al, Human retroviruses and AIDS 1999: a compilation and analysis of nucleic acid and amino acid sequences, eds. Kuiken et al (Theoretical Biology and Biophysics Group, Los Alamos National Laboratory, Los Alamos, New Mexico), pp. 492-505 (2000), Carr et al, Human retroviruses and AIDS 1998: a compilation and analysis of nucleic acid and amino acid sequences, eds. Korber et al (Theoretical

Biology and Biophysics Group, Los Alamos National Laboratory, Los Alamos, New Mexico), pp. III-10-III-19 (1998)). Over 20% of HIV-1 isolates are recombinant in geographic areas where multiple subtypes are common (Robertson et al, Nature 374:124-126 (1995), Cornelissen et al, J. virol. 70:8209-8212 (1996), Dowling et al, AIDS 16:1809-1820 (2002)), and high prevalence rates of recombinant viruses may further complicate the design of experimental HIV-1 immunogens.

To overcome these challenges in AIDS vaccine development, three computer models (consensus, ancestor and center of the tree) have been used to generate centralized HIV-1 genes to (Gaschen et al, Science 296:2354-2360 (2002), Gao et al, Science 299:1517-1518 (2003), Nickle et al, Science 299:1515-1517 (2003), Novitsky et al, J. Virol. 76:5435-5451 (2002), Ellenberger et al, Virology 302:155-163 (2002), Korber et al, Science 288:1789-1796 (2000)). The biology of HIV gives rise to star-like phylogenies, and as a consequence of this, the three kinds of sequences differ from each other by 2 - 5% (Gao et al, Science 299:1517-1518 (2003)). Any of the three centralized gene strategies will reduce the protein distances between immunogens and field virus strains. Consensus sequences minimize the degree of sequence dissimilarity between a vaccine strain and contemporary circulating viruses by creating artificial sequences based on the most common amino acid in each position in an alignment (Gaschen et al, Science 296:2354-2360 (2002)).

Ancestral sequences are similar to consensus sequences but are generated using maximum-likelihood phylogenetic analysis methods (Gaschen et al, Science 296:2354-2360 (2002), Nickle et al, Science 299:1515-1517 (2003)) . In doing so, this method recreates the hypothetical ancestral genes of the analyzed current wild-type sequences (Figure 26). Nickle et al proposed another method to generate centralized HIV-1 sequences, center of the tree (COT), that is similar to ancestral sequences but less influenced by outliers (Science 299:1515-1517 (2003)).

The present invention results, at least in part, from the results of studies designed to determine if centralized immunogens can induce both T and B cell immune responses in animals. These studies involved the generation of an artificial group M consensus *env* gene (CON6), and construction of DNA plasmids and recombinant vaccinia viruses to express CON6 envelopes as soluble gp120 and gp140CF proteins. The results demonstrate that CON6 Env proteins are biologically functional, possess linear, conformational and glycan-dependent epitopes of wild-type HIV-1, and induce cytokine-producing T cells that recognize T cell epitopes of both HIV subtypes B and C. Importantly, CON6 gp120 and gp140CF proteins induce antibodies that neutralize subsets of subtype B and C HIV-1 primary isolates.

The iterative nature of study of the centralized HIV-1 gene approach is derived from the rapidly expanding evolution of HIV-1 sequences, and

the fact that sequences collected in the HIV sequence database (that is, the Los Alamos National Database) are continually being updated with new sequences each year. The CON6 gp120 envelope gene derives from Year 1999 Los Alamos National Database sequences, and Con-S derives from Year 2000 Los Alamos National Database sequences. In addition, CON6 has Chinese subtype C V1, V2, V4, and V5 Env sequences, while Con-S has all group M consensus Env constant and variable regions, that have been shortened to minimal-length variable loops. Codon-optimized genes for a series of Year 2003 group M and subtype consensus sequences have been designed, as have a corresponding series of wild-type HIV-1 Env genes for comparison, for use in inducing broadly reactive T and B cell responses to HIV-1 primary isolates.

SUMMARY OF THE INVENTION

The present invention relates to an immunogen for inducing antibodies that neutralize a wide spectrum of HIV primary isolates and/or to an immunogen that induces a T cell immune response, and to nucleic acid sequences encoding same. The invention also relates to a method of inducing anti-HIV antibodies, and/or to a method of inducing a T cell immune response, using such an immunogen.

Objects and advantages of the present invention will be clear from the description that follows.

BRIEF DESCRIPTION OF THE DRAWINGS

Figures 1A-1D: Generation and expression of the group M consensus *env* gene (CON6). The complete amino acid sequence of CON6 gp160 is shown. (Fig. 1A) The five regions from the wild-type CRF08_BC (98CN006) *env* gene are indicated by underlined letters. Variable regions are indicated by brackets above the sequences. Potential N-liked glycosylation sites are highlighted with bold-faced letters. (Fig. 1B) Constructs of CON6 gp120 and gp140CF. CON6 gp120 and gp140CF plasmids were engineered by introducing a stop codon after the gp120 cleavage site or before the transmembrane domain, respectively. The gp120/gp41 cleavage site and fusion domain of gp41 were deleted in the gp140CF protein. (Fig.1C) Expression of CON6 gp120 and gp140CF. CON6 gp120 and gp140CF were purified from the cell culture supernatants of rVV-infected 293T cells with *galanthus Nivalis argarose* lectin columns. Both gp120 and gp140CF were separated on a 10% SDS-polyarylamide gel and stained with Commassie blue. (Fig. 1D.) CON6 *env* gene optimized based on codon usage for highly expressed human genes.

Figures 2A-2E. Binding of CON6 gp120 gp140 CF to soluble CD4 (sCD4) and anti-Env mAbs. (Figs. 2A-2B) Each of the indicated mabs and sCD4 was covalently immobilized to a CM5 sensor chip (BIAcore) and CON6 gp120 (Fig. 2A) or gp140CF (Fig.

2B) (100 μg/ml and 300 μg/ml, respectively) were injected over each surface. Both gp120 and gp140CF proteins reacted with each anti-gp120 mabs tested except for17b mab, which showed negligible binding to both CON6 gp120 and gp140CF. To determine induction of 17b mab binding to CON6 gp120 and gp140CF, CON6 gp120 (Fig. 2C) or gp140CF (Fig. 2D) proteins were captured (400-580 RU) on individual flow cells immobilized with sCD4 or mabs A32 or T8. Following stabilization of each of the surface, mAb 17b was injected and flowed over each of the immobilized flow cells. Overlay of curves show that the binding of mab 17b to CON6 Env proteins was markedly enhanced on both sCD4 and mab A32 surfaces but not on the T8 surface (Figs. 2C-2D). To determine binding of CON6 gp120 and gp140CF to human mabs in ELISA, stock solutions of 20μg/ml of mabs 447, F39F, A32, IgG1b12 and 2F5 on CON6 gp120 and gp140CF were tittered (Fig. 2E). Mabs 447 (V3), F39F (V3) A32 (gp120) and IgG1b12 (CD4 binding site) each bound to both CON6 gp120 and 140 well, while 2F5 (anti-gp41 ELDKWAS) only bound gp140CF. The concentration at endpoint titer on gp120 for mab 447 and F39F binding was <0.003 μg/ml and 0.006 μg/ml, respectively; for mab A32 was <0.125 μg/ml; for IgG1b12 was <0.002 μg/ml; and for 2F5 was 0.016 μg/ml.

Figures 3A and 3B. Infectivity and coreceptor usage of CON6 envelope. (Fig. 3A) CON6 and control

env plasmids were cotransfected with HIV-1/SG3Δenv backbone into human 293T cells to generate Env-pseudovirions. Equal amounts of each pseudovirion (5 ng p24) were used to infect JC53-BL cells. The infectivity was determined by counting the number of blue cells (infectious units, IU) per microgram of p24 of pseudovirons (IU/μg p24) after staining the infected cells for β-gal expression. (Fig. 3B) Coreceptor usage of the CON6 *env* gene was determined on JC53BL cells treated with AMD3100 and/or TAK-799 for 1 hr (37°C) then infected with equal amounts of p24 (5 ng) of each Env-pseudovirion. Infectivity in the control group (no blocking agent) was set as 100%. Blocking efficiency was expressed as the percentage of IU from blocking experiments compared to those from control cultures without blocking agents. Data shown are mean ± SD.

Figure 4. Western blot analysis of multiple subtype Env proteins against multiple subtype antisera. Equal amount of Env proteins (100 ng) were separated on 10% SDS-polyacrylamide gels. Following electrophoresis, proteins were transferred to Hybond ECL nitrocellulose membranes and reacted with sera from HIV-1 infected patients (1:1,000) or guinea pigs immunized with CON6 gp120 DNA prime, rVV boost (1:1,000). Protein-bound antibody was probed with fluorescent-labeled secondary antibodies and the images scanned and recorded on an infrared imager Odyssey (Li-Cor, Lincoln, NE). Subtypes are

indicated by single-letters after Env protein and serum IDs. Four to six sera were tested for each subtype, and reaction patterns were similar among all sera from the same subtype. One representative result for each subtype serum is shown.

Figure 5. T cell immune responses induced by CON6 Env immunogens in mice. Splenocytes were isolated from individual immunized mice (5 mice/group). After splenocytes were stimulated *in vitro* with overlapping Env peptide pools of CON6 (black column), subtype B (hatched column), subtype C (white column), and medium (no peptide; gray column), INF-γ producing cells were determined by the ELISPOT assay. T cell IFN-γ responses induced by either CON6 gp120 or gp140CF were compared to those induced by subtype specific Env immunogens (JRFL and 96ZM651). Total responses for each envelope peptide pool are expressed as SFCs per million splenocytes. The values for each column are the mean ± SEM of IFN-γ SFCs (n=5 mice/group).

Figures 6A-6E. Construction of codon usage optimized subtype C ancestral and consensus envelope genes (Figs. 6A and 6B, respectively). Ancestral and consensus amino acid sequences (Figs. 6C and 6D, respectively) were transcribed to mirror the codon usage of highly expressed human genes. Paired oligonucleotides (80-mers) overlapping by 20 bp were designed to contain 5′ invariant sequences including

the restriction enzyme sites EcoRI, BbsI, Bam HI and BsmBI. BbsI and BsmBI are Type II restriction enzymes that cleave outside of their recognition sequences. Paired oligomers were linked individually using PCR and primers complimentary to the 18 bp invariant sequences in a stepwise fashion, yielding 140bp PCR products. These were subcloned into pGEM-T and sequenced to confirm the absence of inadvertant mutations/deletions. Four individual pGEM-T subclones containing the proper inserts were digested and ligated together into pcDNA3.1. Multi-fragment ligations occurred repeatly amongst groups of fragments in a stepwise manner from the 5' to the 3' end of the gene until the entire gene was reconstructed in pcDNA3.1. (See schematic in Fig. 6E.)

Figure 7. JC53-BL cells are a derivative of HeLa cells that express high levels of CD4 and the HIV-1 coreceptors CCR5 and CXCR4. They also contain the reporter cassettes of luciferase and β-galactosidase that are each expressed from an HIV-1 LTR. Expression of the reporter genes is dependent on production of HIV-1 Tat. Briefly, cells are seeded into 24 or 96-well plates, incubated at 37°C for 24 hours and treated with DEAE-Dextran at 37°C for 30 minutes. Virus is serially diluted in 1% DMEM, added to the cells incubating in DEAE-Dextran, and allowed to incubate for 3 hours at 37°C after which an additional cell media is added to each

well. Following a final 48-hour incubation at 37°C, cells are either fixed, stained using X-Gal to visualize β-galactosidase expressing blue foci or frozen-thawed three times to measure luciferase activity.

Figure 8. Sequence alignment of subtype C ancestral and consensus *env* genes. Alignment of the subtype C ancestral (bottom line) and consensus (top line) *env* sequences showing a 95.5% sequence homology; amino acid sequence differences are indicated. One noted difference is the addition of a glycosylation site in the C ancestral *env* gene at the base of the V1 loop. A plus sign indicates a within-class difference of amino acid at the indicated position; a bar indicates a change in the class of amino acid. Potential N-glycosylation sites are marked in blue. The position of truncation for the gp140 gene is also shown.

Figure 9. Expression of subtype C ancestral and consensus envelopes in 293T cells. Plasmids containing codon-optimized *gp160, gp140, or gp120* subtype C ancestral and consensus genes were transfected into 293T cells, and protein expression was examined by Western Blot analysis of cell lysates. 48-hours post-transfection, cell lysates were collected, total protein content determined by the BCA protein assay, and 2 μg of total protein was loaded per lane on a 4-20% SDS-PAGE gel. Proteins

were transferred to a PVDF membrane and probed with HIV-1 plasma from a subtype C infected patient.

Figures 10A and 10B. Fig. 10A. *Trans* complementation of *env*-deficient HIV-1 with codon-optimized subtype C ancestral and consensus gp160 and gp140. Plasmids containing codon-optimized, subtype C ancestral or consensus *gp160* or *gp140* genes were co-transfected into 293T cells with an HIV-1/SG3Δ*env* provirus. 48 hours post-transfection cell supernatants containing pseudotyped virus were harvested, clarified by centrifugation, filtered through at 0.2μM filter, and pelleted through a 20% sucrose cushion. Quantification of p24 in each virus pellet was determined using the Coulter HIV-1 p24 antigen assay; 25ng of p24 was loaded per lane on a 4-20% SDS-PAGE gel for particles containing a codon-optimized envelope. 250ng of p24 was loaded per lane for particles generated by co-transfection of a rev-dependent wild-type subtype C 96ZAM651*env* gene. Differences in the amount of p24 loaded per lane were necessary to ensure visualization of the rev-dependent envelopes by Western Blot. Proteins were transferred to a PVDF membrane and probed with pooled plasma from HIV-1 subtype B and subtype C infected individuals. Fig. 10B. Infectivity of virus particles containing subtype C ancestral and consensus envelope glycoproteins. Infectivity of pseudotyped virus containing ancestral or consensus *gp160* or *gp140* envelope was determined using the

JC53-BL assay. Sucrose cushion purified virus particles were assayed by the Coulter p24 antigen assay, and 5-fold serial dilutions of each pellet were incubated with DEAE-Dextran treated JC53-BL cells. Following a 48-hour incubation period, cells were fixed and stained to visualize β-galactosidase expressing cells. Infectivity is represented as infectious units per ng of p24 to normalize for differences in the concentration of the input pseudovirions.

Figure 11. Co-receptor usage of subtype C ancestral and consensus envelopes. Pseudotyped particles containing ancestral or consensus envelope were incubated with DEAE-Dextran treated JC53-BL cells in the presence of AMD3100 (a specific inhibitor of CXCR4), TAK779 (a specific inhibitor of CCR5), or AMD3000+TAK779 to determine co-receptor usage. NL4.3, an isolate known to utilize CXCR4, and YU-2, a known CCR5-using isolate, were included as controls.

Figures 12A-12C. Neutralization sensitivity of subtype C ancestral and consensus envelope glycoproteins. Equivalent amounts of pseudovirions containing the ancestral, consensus or 96ZAM651 *gp160* envelopes (1,500 infectious units) were pre-incubated with a panel of plasma samples from HIV-1 subtype C infected patients and then added to the JC53-BL cell monolayer in 96-well plates. Plates

were cultured for two days and luciferase activity was measured as an indicator of viral infectivity. Virus infectivity is calculated by dividing the luciferase units (LU) produced at each concentration of antibody by the LU produced by the control infection. The mean 50% inhibitory concentration (IC_{50}) and the actual % neutralization at each antibody dilution are then calculated for each virus. The results of all luciferase experiments are confirmed by direct counting of blue foci in parallel infections.

Figures 13A-13F. Protein expression of consensus subtype C Gag (Fig. 13A) and Nef (Fig. 13B) following transfection into 293T cells. Consensus subtype C Gag and Nef amino acid sequences are set forth in Figs. 13C and 13D, respectively, and encoding sequences are set forth in Figs. 13E and 13F, respectively.

Figures 14A-14C. Figs. 14A and 14B show the Con-S Env amino acid sequence and encoding sequence, respectively. Fig. 14C shows expression of Group M consensus Con-S Env proteins using an *in vitro* transcription and translation system.

Figures 15A and 15B. Expression of Con-S *env* gene in mammalian cells. (Fig. 15A - cell lysate, Fig. 15B - supernatant.)

Figures 16A and 16B. Infectivity (Fig. 16A) and coreceptor usage (Fig. 16B) of CON6 and Con-S *env* genes.

Figures 17A-17C. Env protein incorporation in CON6 and Con-S Env-pseudovirions. (Fig. 17A - lysate, Fig. 17B - supernatant, Fig. 17C pellet.)

Figures 18A-18D. Figs. 18A and 18B show subtype A consensus Env amino acid sequence and nucleic acid sequence encoding same, respectively. Figs. 18C and 18D show expression of A.con *env* gene in mammalian cells (Fig. 18C - cell lysate, Fig. 18D - supernatant).

Figures 19A-19H. M.con.gag (Fig. 19A), M.con.pol (Fig. 19B), M.con.nef (Fig. 19C) and C.con.pol (Fig. 19D) nucleic acid sequences and corresponding encoded amino acid sequences (Figs. 19E-19H, respectively).

Figures 20A-20D. Subtype B consensus *gag* (Fig. 20A) and *env* (Fig.20B) genes. Corresponding amino acid sequences are shown in Figs. 20C and 20D.

Figure 21. Expression of subtype B consensus *env* and *gag* genes in 293T cells. Plasmids containing codon-optimized subtype B consensus *gp160*, *gp140*, and *gag* genes were transfected into 293T cells, and protein expression was examined by

Western Blot analysis of cell lysates. 48-hours post-transfection, cell lysates were collected, total protein content determined by the BCA protein assay, and 2 μg of total protein was loaded per lane on a 4-20% SDS-PAGE gel. Proteins were transferred to a PVDF membrane and probed with serum from an HIV-1 subtype B infected individual.

Figure 22. Co-receptor usage of subtype B consensus envelopes. Pseudotyped particles containing the subtype B consensus gp160 Env were incubated with DEAE-Dextran treated JC53-BL cells in the presence of AMD3100 (a specific inhibitor of CXCR4), TAK779 (a specific inhibitor of CCR5), and AMD3000+TAK779 to determine co-receptor usage. NL4.3, an isolate known to utilize CXCR4 and YU-2, a known CCR5-using isolate, were included as controls.

Figures 23A and 23B. *Trans* complementation of *env*-deficient HIV-1 with codon-optimized subtype B consensus *gp160* and *gp140* genes. Plasmids containing codon-optimized, subtype B consensus *gp160* or *gp140* genes were co-transfected into 293T cells with an HIV-1/SG3Δenv provirus. 48-hours post-transfection cell supernatants containing pseudotyped virus were harvested, clarified in a tabletop centrifuge, filtered through a 0.2μM filter, and pellet through a 20% sucrose cushion. Quantification of p24 in each virus pellet was determined using the Coulter HIV-1 p24 antigen

assay; 25 ng of p24 was loaded per lane on a 4-20% SDS-PAGE gel. Proteins were transferred to a PVDF membrane and probed with anti-HIV-1 antibodies from infected HIV-1 subtype B patient serum. *Trans* complementation with a rev-dependent NL4.3 *env* was included for control. Figure 23B. Infectivity of virus particles containing the subtype B concensus envelope. Infectivitiy of pseudotyped virus containing consensus B gp160 or gp140 was determined using the JC53-BL assay. Sucrose cushion purified virus particles were assayed by the Coulter p24 antigen assay, and 5-fold serial dilutions of each pellet were incubated with DEAE-Dextran treated JC53-BL cells. Following a 48-hour incubation period, cells were fixed and stained to visualize β-galactosidase expressing cells. Infectivity is expressed as infectious units per ng of p24.

Figures 24A-24D. Neutralization sensitivity of virions containing subtype B consensus gp160 envelope. Equivalent amounts of pseudovirions containing the subtype B consensus or NL4.3 Env (gp160) (1,500 infectious units) were preincubated with three different monoclonal neutralizing antibodies and a panel of plasma samples from HIV-1 wubtype B infected individuals, and then added to the JC53-BL cell monolayer in 96-well plates. Plates were cultured for two days and luciferase activity was measured as an indicator of viral infectivity. Virus infectivity was calculated by

dividing the luciferase units (LU) produced at each concentration of antibody by the LU produced by the control infection. The mean 50% inhibitory concentration (IC_{50}) and the actual % neutralization at each antibody dilution were then calculated for each virus. The results of all luciferase experiments were confirmed by direct counting of blue foci in parallel infections. Fig. 24A. Neutralization of Pseudovirions containing Subtype B consensus Env (gp160). Fig. 24B. Neutralization of Pseudovirions containing NL4.3 Env (gp160). Fig. 24C. Neutralization of Pseudovirions containing Subtype B consensus Env (gp160). Fig. 24D. Neutralization of Pseudovirions containing NL4.3 Env (gp160).

Figures 25A and 25B. Fig. 25A. Density and p24 analysis of sucrose gradient fractions. 0.5ml fractions were collected from a 20-60% sucrose gradient. Fraction number 1 represents the most dense fraction taken from the bottom of the gradient tube. Density was measured with a refractometer and the amount of p24 in each fraction was determined by the Coulter p24 antigen assay. Fractions 6-9, 10-15, 16-21, and 22-25 were pooled together and analyzed by Western Blot. As expected, virions sedimented at a density of 1.16-1.18 g/ml. Fig. 25B. VLP production by co-transfection of subtype B consensus *gag* and *env* genes. 293T cells were co-transfected with subtype B consensus *gag* and

env genes. Cell supernatants were harvested 48-hours post-transfection, clarified through at 20% sucrose cushion, and further purified through a 20-60% sucrose gradient. Select fractions from the gradient were pooled, added to 20ml of PBS, and centrifuged overnight at 100,000 x g. Resuspended pellets were loaded onto a 4-20% SDS-PAGE gel, proteins were transferred to a PVDF membrane, and probed with plasma from an HIV-1 subtype B infected individual.

Figures 26A and 26B. Fig. 26A. 2000 Con-S 140CFI.ENV. Fig. 26B. Codon-optimized Year 2000 Con-S 140CFI.seq.

Figure 27. Individual C57BL/6 mouse T cell responses to HIV-1 envelope peptides. Comparative immunogenicity of CON6 gp140CFI and Con-S gp140CFI in C57BL/C mice. Mice were immunized with either HIV5305 (Subtype A), 2801 (Subtype B), CON6 or Con-S Envelope genes in DNA prime, rVV boost regimens, 5 mice per group. Spleen cells were assayed for IFN-γ spot-forming cells 10 days after rVV boost, using mixtures of overlapping peptides from Envs of HIV-1 UG37(A), MN(B), Ch19(C), 89.6(B) SF162(B) or no peptide negative control.

Figures 28A-28C. Fig. 28A. Con-B 2003 Env. pep (841 a.a.). Amino acid sequence underlined is the fusion domain that is deleted in 140CF design and

the "W" underlined is the last amino acid at the C-terminus, all amino acids after the "W" are deleted in the 140CF design. Fig. 28B. Con-B-140CF.pep (632 a.a.). Amino acids in bold identify the junction of the deleted fusion cleavage site. Fig. 28C. Codon-optimized Con-B 140CF.seq (1927 nt.).

Figures 29A-29C. Fig. 29A. CON_OF_CONS-2003 (829 a.a.). Amino acid sequence underlined is the fusion domain that is deleted in 140CF design and the "W" underlined is the last amino acid at the C-terminus, all amino acids after the "W" are deleted in the 140CF design. Fig. 29B. ConS-2003 140CF.pep (620 a.a.). Amino acids in bold identify the junction of the deleted fusion cleavage site. Fig. 29C. CODON-OPTIMIZED ConS-2003 140CF.seq (1891 nt.).

Figures 30A-30C. Fig. 30A. CONSENSUS_A1-2003 (845 a.a.). Amino acid sequence underlined is the fusion domain that is deleted in 140CF design and the "W" underlined is the last amino acid at the C-terminus, all amino acids after the "W" are deleted in the 140CF design. Fig. 30B. Con-A1-2003 140CF.pep (629 a.a.). Amino acids in bold identify the junction of the deleted fusion cleavage site. Fig. 30C. CODON-OPTIMIZED Con-A1-2003.seq.

Figures 31A-31C. Fig. 31A. CONSENSUS_C-2003 (835 a.a.). Amino acid sequence underlined is the fusion domain that is deleted in 140CF design and the "W" underlined is the last amino acid at the C-terminus, all amino acids after the "W" are deleted in the 140CF design. Fig. 31B. Con-C 2003 140CF.pep (619 a.a.). Amino acids in bold identify the junction of the deleted fusion cleavage site. Fig. 31C. CODON-OPTIMIZED Con-C-2003 (140 CF (1,888 nt.).

Figures 32A-32C. Fig. 32A. CONSENSUS_G-2003 (842 a.a.). Amino acid sequence underlined is the fusion domain that is deleted in 140CF design and the "W" underlined is the last amino acid at the C-terminus, all amino acids after the "W" are deleted in the 140CF design. Fig. 32B. Con-G-2003 140CF.pep (626 a.a.). Amino acids in bold identify the junction of the deleted fusion cleavage site. Fig. 32C. CODON-OPTIMIZED Con-G-2003.seq.

Figures 33A-33C. Fig. 33A. CONSENSUS_01_AE-2003 (854 a.a.). Amino acid sequence underlined is the fusion domain that is deleted in 140CF design and the "W" underlined is the last amino acid at the C-terminus, all amino acids after the "W" are deleted in the 140CF design. Fig. 33B. Con-AE01-2003 140CF.pep (638 a.a.). Amino acids in bold identify the junction of the deleted fusion cleavage

site. Fig. 33C. CODON-OPTIMIZED Con-AE01-2003.seq. (1945 nt.).

Figures 34A-34C. Fig. 34A. Wild-type subtype A Env. 00KE_MSA4076-A (Subtype A, 891 a.a.). Amino acid sequence underlined is the fusion domain that is deleted in 140CF design and the "W" underlined is the last amino acid at the C-terminus, all amino acids after the "W" are deleted in the 140CF design. Fig. 34B. 00KE_MSA4076-A 140CF.pep (647 a.a.). Amino acids in bold identify the junction of the deleted fusion cleavage site. Fig. 34C. CODON-OPTIMIZED 00KE_MSA4076-A 140CF.seq. (1972 nt.).

Figures 35A-35C. Fig. 35A. Wild-type subtype B. QH0515.1g gp160 (861 a.a.). Amino acid sequence underlined is the fusion domain that is deleted in 140CF design and the "W" underlined is the last amino acid at the C-terminus, all amino acids after the "W" are deleted in the 140CF design. Fig. 35B. QH0515.1g 140CF (651 a.a.). Amino acids in bold identify the junction of the deleted fusion cleavage site. Fig. 35C. CODON-OPTIMIZED QH0515.1g 140CF.seq (1984 nt.).

Figures 36A-36C. Fig. 36A. Wild-type subtype C. DU123.6 gp160 (854 a.a.). Amino acid sequence underlined is the fusion domain that is deleted in 140CF design and the "W" underlined is the last amino acid at the C-terminus, all amino acids after

the "W" are deleted in the 140CF design. Fig. 36B. DU123.6 140CF (638 a.a.). Amino acids in bold identify the junction of the deleted fusion cleavage site. Fig. 36C. CODON-OPTIMIZED DU123.6 140CF.seq (1945 nt.).

Figures 37A-37C. Fig. 37A. Wild-type subtype CRF01_AE. 97CNGX2F-AE (854 a.a.). Amino acid sequence underlined is the fusion domain that is deleted in 140CF design and the "W" underlined is the last amino acid at the C-terminus, all amino acids after the "W" are deleted in the 140CF design. Fig. 37B. 97CNGX2F-AE 140CF.pep (629 a.a.). Amino acids in bold identify the junction of the deleted fusion cleavage site. Fig. 37C. CODON-OPTIMIZED 97CNGX2F-AE 140CF.seq (1921 nt.).

Figures 38A-38C. Fig. 38A. Wild-type DRCBL-G (854 a.a.). Amino acid sequence underlined is the fusion domain that is deleted in 140CF design and the "W" underlined is the last amino acid at the C-terminus, all amino acids after the "W" are deleted in the 140CF design. Fig. 38B. DRCBL-G 140CF.pep (630 a.a.). Amino acids in bold identify the junction of the deleted fusion cleavage site. Fig. 38C. CODON-OPTIMIZED DRCBL-G 140CF.seq (1921 nt.).

Figures 39A and 39B. Fig. 39A. 2003 Con-S Env. Fig. 39B. 2003 Con-S Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.)

Figures 40A and 40B. Fig. 40A. 2003 M. Group.Anc Env. Fig. 40B. 2003 M. Group.anc Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.)

Figures 41A and 41B. Fig. 41A. 2003 CON_A1 Env. Fig. 41B. 2003 CON_A1 Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.)

Figures 42A and 42B. Fig. 42A. 2003 A1.Anc Env. Figs. 42B. 2003 A1.anc Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.)

Figures 43A and 43B. Fig. 43A. 2003 CON_A2 Env. Fig. 43B. 2003 CON_A2 Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.)

Figures 44A and 44B. Fig. 44A. 2003 CON_B Env. Fig. 44B. 2003 CON_B Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.)

Figures 45A and 45B. Fig. 45A. 2003 B.anc Env. Figs. 45B. 2003 B.anc Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.)

Figures 46A and 46B. Fig. 46A. 2003 CON_C Env. Fig. 46B. 2003 CON_C Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.)

Figures 47A and 47B. Fig. 47A. 2003 C.anc Env. Fig. 47B. 2003 C.anc Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.)

Figures 48A and 48B. Fig. 48A. 2003 CON_D Env. Fig. 48B. 2003 CON_D Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.)

Figures 49A and 49B. Fig. 49A. 2003 CON_F1 Env. Fig. 49B. 2003 CON_F1 Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.)

Figures 50A and 50B. Fig. 50A. 2003 CON_F2 Env. Fig. 50B. 2003 CON_F2 Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.)

Figures 51A and 51B. Fig. 51A. 2003 CON_G Env. Fig. 51B. 2003 CON_G Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.)

Figures 52A and 52B. Fig. 52A. 2003 CON_H Env. Fig. 52B. 2003 CON_H Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.)

Figures 53A and 53B. Fig. 53A. 2003 CON_01_AE Env. Fig. 53B. 2003 CON_01_AE Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.)

Figures 54A and 54B. Fig. 54A. 2003 CON_02_AG Env. Fig. 54B. 2003 CON_02_AG Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.)

Figures 55A and 55B. Fig. 55A. 2003 CON_03_AB Env. Fig. 55B. 2003 CON_03_AB Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.)

Figures 56A and 56B. Fig. 56A. 2003 CON_04_CPX Env. Fig. 56B. 2003 CON_04_CPX Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.)

Figures 57A and 57B. Fig. 57A. 2003 CON_06_CPX Env. Fig. 57B. 2003 CON_06_CPX Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.)

Figures 58A and 58B. Fig. 58A. 2003 CON_08_BC Env. Fig. 58B. 2003 CON_08_BC Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.)

Figures 59A and 59B. Fig. 59A. 2003 CON_10_CD Env. Fig. 59B. 2003 CON_10_CD Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.)

Figures 60A and 60B. Fig. 60A. 2003 CON_11_CPX Env. Fig. 60B. 2003 CON_11_CPX Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.)

Figures 61A and 61B. Fig. 61A. 2003 CON_12_BF Env. Fig. 61B. 2003 CON_12_BF Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.)

Figures 62A and 62B. Fig. 62A. 2003 CON_14_BG Env. Fig. 62B. 2003 CON_14_BG Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.)

Figures 63A and 63B. Fig. 63A. 2003_CON_S gag.PEP. Fig. 63B. 2003_CON_S gag.OPT. (OPT = codon optimized encoding sequence.)

Figures 64A and 64B. Fig. 64A. 2003_M.GROUP.anc gag.PEP. Fig. 64B. 2003_M.GROUP.anc gag.OPT. (OPT = codon optimized encoding sequence.)

Figures 65A-65D. Fig. 65A. 2003_CON_A1 gag.PEP. Fig. 65B. 2003_CON_A1 gag.OPT. Fig. 65C. 2003_A1.anc gag.PEP. Fig. 65D. 2003_A1.anc gag.OPT. (OPT = codon optimized encoding sequence.)

Figures 66A and 66B. Fig. 66A. 2003_CON_A2 gag.PEP. Fig. 66B. 2003_CON_A2 gag.OPT. (OPT = codon optimized encoding sequence.)

Figures 67A-67D. Fig. 67A. 2003_CON_B gag.PEP. Fig. 67B. 2003_CON_B gag.OPT. Fig. 67C. 2003_B.anc gag.PEP. Fig. 67D. 2003_B.anc gag.OPT. (OPT = codon optimized encoding sequence.)

Figures 68A-68D. Fig. 68A. 2003_CON_C gag.PEP. Fig. 68B. 2003_CON_C gag.OPT. Fig. 68C. 2003_C.anc.gag.PEP. Fig. 68D. 2003_C.anc.gag.OPT. (OPT = codon optimized encoding sequence.)

Figures 69A and 69B. Fig. 69A. 2003_CON_D gag.PEP. Fig. 69B. 2003_CON_D gag.OPT. (OPT = codon optimized encoding sequence.)

Figures 70A and 70B. Fig. 70A. 2003_CON_F gag.PEP. Fig. 70B. 2003_CON_F gag.OPT. (OPT = codon optimized encoding sequence.)

Figures 71A and 71B. Fig. 71A. 2003_CON_G gag.PEP. Fig. 71B. 2003_CON_G gag.OPT. (OPT = codon optimized encoding sequence.)

Figures 72A and 72B. Fig. 72A. 2003_CON_H gag.PEP. Fig. 72B. 2003_CON_H gag.OPT. (OPT = codon optimized encoding sequence.)

Figures 73A and 73B. Fig. 73A. 2003_CON_K gag.PEP. Fig. 73B. 2003_CON_K gag.OPT. (OPT = codon optimized encoding sequence.)

Figures 74A and 74B. Fig. 74A. 2003_CON_01_AE gag.PEP. Fig. 7B. 2003_CON_01_AE gag.OPT. (OPT = codon optimized encoding sequence.)

Figures 75A and 75B. Fig. 75A. 2003_CON_02_AG gag.PEP. Fig. 75B. 2003_CON_02_AG gag.OPT. (OPT = codon optimized encoding sequence.)

Figures 76A and 76B. Fig. 76A. 2003_CON_03_ABG gag.PEP. Fig. 76B. 2003_CON_03_ABG gag.OPT. (OPT = codon optimized encoding sequence.)

Figures 77A and 77B. Fig. 77A. 2003_CON_04_CFX gag.PEP. Fig. 77B. 2003 CON_04_CFX gag.OPT. (OPT = codon optimized encoding sequence.)

Figures 78A and 78B. Fig. 78A. 2003_CON_06_CPX gag.PEP. Fig. 78B. 2003_CON_06_CPX gag.OPT. (OPT = codon optimized encoding sequence.)

Figures 79A and 79B. Fig. 79A. 2003_CON_07_BC gag.PEP. Fig. 79B. 2003_CON_07_BC gag.OPT. (OPT = codon optimized encoding sequence.)

Figures 80A and 80B. Fig. 80A. 2003_CON_08_BC gag.PEP. Fig. 80B. 2003_CON_08_BC gag.OPT. (OPT = codon optimized encoding sequence.)

Figures 81A and 81B. Fig. 81A. 2003_CON_10_CD gag.PEP. Fig. 81B. 2003_CON_10_CD gag.OPT. (OPT = codon optimized encoding sequence.)

Figures 82A and 82B. Fig. 82A. 2003_CON_11_CPX gag.PEP. Fig. 82B. 2003_CON_11_CPX gag.OPT. (OPT = codon optimized encoding sequence.)

Figures 83A and 83B. Fig. 83A. 2003_CON_12_BF.gag.PEP. Fig. 83B. 2003_CON_12_BF.gag.OPT. (OPT = codon optimized encoding sequence.)

Figures 84A and 84B. Fig. 84A. 2003_CON_14_BG gag.PEP. Fig. 84B. 2003_CON_14_BG gag.OPT. (OPT = codon optimized encoding sequence.)

Figures 85A and 85B. Fig. 85A. 2003_CONS nef.PEP. Fig. 85B. 2003_CONS nef.OPT. (OPT = codon optimized encoding sequence.)

Figures 86A and 86B. Fig. 86A. 2003_M GROUP.anc nef.PEP. Fig. 86B. 2003_M GROUP.anc.nef.OPT. (OPT = codon optimized encoding sequence.)

Figures 87A and 87B. Fig. 87A. 2003_CON_A nef.PEP. Fig. 87B. 2003_CON_A nef.OPT. (OPT = codon optimized encoding sequence.)

Figures 88A-88D. Fig. 88A. 2003_CON_A1 nef.PEP. Fig. 88B. 2003_CON_A1 nef.OPT. Fig. 88C. 2003_A1.anc nef.PEP. Fig. 88D. 2003_A1.anc nef.OPT. (OPT = codon optimized encoding sequence.)

Figures 89A and 89B. Fig. 89A. 2003_CON_A2 nef.PEP. Fig. 89B. 2003_CON_A2 nef.OPT. (OPT = codon optimized encoding sequence.)

Figures 90A-90D. Fig. 90A. 2003_CON_B nef.PEP. Fig. 90B. 2003_CON-B nef.OPT. Fig. 90C. 2003_B.anc nef.PEP. Fig. 90D. 2003_B.anc nef.OPT. (OPT = codon optimized encoding sequence.)

Figures 91A and 91B. Fig. 91A. 2003_CON_02_AG nef.PEP. Fig. 91B. 2003_CON_02_AG nef.OPT. (OPT = codon optimized encoding sequence.)

Figures 92A-92D. Fig. 92A. 2003_CON_C nef.PEP. Fig. 92B. 2003_CON_C nef.OPT. Fig. 92C. 2003_C.anc nef.PEP. Fig. 92D. 2003_C.anc nef.OPT. (OPT = codon optimized encoding sequence.)

Figures 93A and 93B. Fig. 93A. 2003_CON_D nef.PEP. Fig. 93B. 2003_CON_D nef.OPT. (OPT = codon optimized encoding sequence.)

Figures 94A and 94B. Fig. 94A. 2003_CON_F1 nef.PEP. Fig. 94B. 2003_CON_F1 nef.OPT. (OPT = codon optimized encoding sequence.)

Figures 95A and 95B. Fig. 95A. 2003_CON_F2 nef.PEP. Fig. 95B. 2003_CON_F2 nef.OPT. (OPT = codon optimized encoding sequence.)

Figures 96A and 96B. Fig. 96A. 2003_CON_G nef.PEP. Fig. 96B. 2003_CON_G nef.OPT. (OPT = codon optimized encoding sequence.)

Figures 97A and 97B. Fig. 97A. 2003_CON_H nef.PEP. Fig. 97B. 2003_CON_H nef.OPT. (OPT = codon optimized encoding sequence.)

Figures 98A and 98B. Fig. 98A. 2003_CON_01_AE nef.PEP. Fig. 98B. 2003_CON_01_AE nef.OPT. (OPT = codon optimized encoding sequence.)

Figures 99A and 99B. Fig. 99A. 2003_CON_03_AE nef.PEP. Fig. 99B. 2003_CON_03_AE nef.OPT. (OPT = codon optimized encoding sequence.)

Figures 100A and 100B. Fig. 100A. 2003_CON_04_CFX nef.PEP. Fig. 100B. 2003_CON_04_CFX nef.OPT. (OPT = codon optimized encoding sequence.)

Figures 101A and 101B. Fig. 101A. 2003_CON_06_CFX nef.PEP. Fig. 101B. 2003_CON_06_CFX nef.OPT. (OPT = codon optimized encoding sequence.)

Figures 102A and 102B. Fig. 102A. 2003_CON_08_BC nef.PEP. Fig. 102B. 2003_CON_08_BC nef.OPT. (OPT = codon optimized encoding sequence.)

Figures 103A and 103B. Fig. 103A. 2003_CON_10_CD nef.PEP. Fig. 103B. 2003_CON_10_CD nef.OPT. (OPT = codon optimized encoding sequence.)

Figures 104A and 104B. Fig. 104A. 2003_CON_11_CFX nef.PEP. Fig. 104B. 2003_CON_11_CFX nef.OPT. (OPT = codon optimized encoding sequence.)

Figures 105A and 105B. Fig. 105A. 2003_CON_12_BF nef.PEP. Fig. 105B. 2003_CON_12_BF nef.OPT. (OPT = codon optimized encoding sequence.)

Figures 106A and 106B. Fig. 106A. 2003_CON_14_BG nef.PEP. Fig. 106B. 2003_CON_14_BG nef.OPT. (OPT = codon optimized encoding sequence.)

Figures 107A and 107B. Fig. 107A. 2003_CON_S pol.PEP. Fig. 107B. 2003_CON_S pol.OPT. (OPT = codon optimized encoding sequence.)

Figures 108A and 108B. Fig. 108A. 2003_M GROUP anc pol.PEP. Fig. 108B. 2003_M.GROUP anc pol.OPT. (OPT = codon optimized encoding sequence.)

Figures 109A-109D. Fig. 109A. 2003_CON_A1 pol.PEP. Fig. 109B. 2003_CON_A1 pol.OPT. Fig. 109C. 2003_A1.anc pol.PEP. Fig. 109D. 2003_A1.anc pol.OPT. (OPT = codon optimized encoding sequence.)

Figures 110A and 110B. Fig. 110A. 2003_CON_A2 pol.PEP. Fig. 110B. 2003_CON_A2 pol.OPT. (OPT = codon optimized encoding sequence.)

Figures 111A-111D. Fig. 111A. 2003_CON_B pol.PEP. Fig. 111B. 2003_CON_B pol.OPT. Fig. 111C. 2003_B.anc pol.PEP. Fig. 111D. 2003_B.anc pol.OPT. (OPT = codon optimized encoding sequence.)

Figures 112A-112D. Fig. 112A. 2003_CON_C pol.PEP. Fig. 112B. 2003_CON_C pol.OPT.

Fig. 112C. 2003_C.anc pol.PEP. Fig. 112D. 2003_C.anc pol.OPT. (OPT = codon optimized encoding sequence.)

Figures 113A and 113B. Fig. 113A. 2003_CON_D pol.PEP. Fig. 113B. 2003_CON_D pol.OPT. (OPT = codon optimized encoding sequence.)

Figures 114A and 114B. Fig. 114A. 2003_CON_F1 pol.PEP. Fig. 114B. 2003_CON_F1 pol.OPT. (OPT = codon optimized encoding sequence.)

Figures 115A and 115B. Fig. 115A. 2003_CON_F2 pol.PEP. Fig. 115B. 2003_CON_F2 pol.OPT. (OPT = codon optimized encoding sequence.)

Figures 116A and 116B. Fig. 116A. 2003_CON_G pol.PEP. Fig. 116B. 2003_CON_G pol.OPT. (OPT = codon optimized encoding sequence.)

Figures 117A and 117B. Fig. 117A. 2003_CON_H pol.PEP. Fig. 117B. 2003_CON_H pol.OPT. (OPT = codon optimized encoding sequence.)

Figures 118A and 118B. Fig. 118A. 2003_CON_01_AE pol.PEP. Fig. 118B. 2003_CON_01_AE pol.OPT. (OPT = codon optimized encoding sequence.)

Figures 119A and 119B. Fig. 119A. 2003_CON_02_AG pol.PEP. Fig. 119B. 2003_CON_02_AG pol.OPT. (OPT = codon optimized encoding sequence.)

Figures 120A and 120B. Fig. 120A. 2003_CON_03_AB pol.PEP. Fig. 120B. 2003_CON_03_AB pol.OPT. (OPT = codon optimized encoding sequence.)

Figures 121A and 121B. Fig. 121A. 2003_CON_04_CPX pol.PEP. Fig. 121B. 2003_CON_04_CPX pol.OPT. (OPT = codon optimized encoding sequence.)

Figures 122A and 122B. Fig. 122A. 2003_CON_06_CPX pol.PEP. Fig. 122B. 2003_CON_06_CPX pol.OPT. (OPT = codon optimized encoding sequence.)

Figures 123A and 123B. Fig. 123A. 2003_CON_08_BC pol.PEP. Fig. 123B. 2003_CON_08_BC pol.OPT. (OPT = codon optimized encoding sequence.)

Figures 124A and 124B. Fig. 124A. 2003_CON_10_CD pol.PEP. Fig. 124B. 2003_CON_10_CD pol.OPT. (OPT = codon optimized encoding sequence.)

Figures 125A and 125B. Fig. 125A. 2003_CON_11_CPX pol.PEP. Fig. 125B.

2003_CON_11_CPX pol.OPT. (OPT = codon optimized encoding sequence.)

Figures 126A and 126B. Fig. 126A. 2003_CON_12_BF pol.PEP. Fig. 126B. 2003_CON_12_BF pol.OPT. (OPT = codon optimized encoding sequence.)

Figures 127A and 127B. Fig. 127A. 2003_CON_14_BG pol.PEP. Fig. 127B. 2003_CON_14_BG pol.OPT. (OPT = codon optimized encoding sequence.)

DETAILED DESCRIPTION OF THE INVENTION

The present invention relates to an immunogen that induces antibodies that neutralize a wide spectrum of human immunodeficiency virus (HIV) primary isolates and/or that induces a T cell response. The immunogen comprises at least one consensus or ancestral immunogen (e.g., Env, Gag, Nef or Pol), or portion or variant thereof. The invention also relates to nucleic acid sequences encoding the consensus or ancestral immunogen, or portion or variant thereof. The invention further relates to methods of using both the immunogen and the encoding sequences. While the invention is described in detail with reference to specific consensus and ancestral immunogens (for example, to a group M consensus Env), it will be appreciated that the approach described herein can be used to generate a variety of consensus or ancestral

immunogens (for example, envelopes for other HIV-1 groups (e.g., N and O)).

In accordance with one embodiment of the invention, a consensus *env* gene can be constructed by generating consensus sequences of *env* genes for each subtype of a particular HIV-1 group (group M being classified into subtypes A-D, F-H, J an K), for example, from sequences in the Los Alamos HIV Sequence Database (using, for example, MASE (Multiple Aligned Sequence Editor)). A consensus sequence of all subtype consensuses can then be generated to avoid heavily sequenced subtypes (Gaschen et al, Science 296:2354-2360 (2002), Korber et al, Science 288:1789-1796 (2000)). In the case of the group M consensus *env* gene described in Example 1 (designated CON6), five highly variable regions from a CRF08_BC recombinant strain (98CN006) (V1, V2, V4, V5 and a region in cytoplasmic domain of gp41) are used to fill in the missing regions in the sequence (see, however, corresponding regions for Con-S). For high levels of expression, the codons of consensus or ancestral genes can be optimized based on codon usage for highly expressed human genes (Haas et al, Curr. Biol. 6:315-324 (2000), Andre et al, J. Virol. 72:1497-1503 (1998)).

With the Year 1999 consensus group M *env* gene, CON6, it has been possible to demonstrate induction of superior T cell responses by CON6 versus wild-type B and C *env* by the number of ELISPOT γ-interferon spleen spot forming cells and the

number of epitopes recognized in two strains of mice (Tables 1 and 2 show the data in BALB/c mice). The ability of CON6 Env protein to induce neutralizing antibodies to HIV-1 primary isolates has been compared to that of several subtype B Env. The target of neutralizing antibodies induced by CON6 includes several non-B HIV-1 strains.

Table 1. T cell epitope mapping of CON6, JRFL and 96ZM651 Env immunogen in BALB/c mice

Peptide		Immunogen			T cell response
		CON6	JRFL (B)	96ZM651 (C)	
CON 6 (group M consensus)					
16	DTEVHNVWATHACVP	+		+	CD4
48 49	KNSSEYYRLINCNTS EYYRLINCNTSAITQ	+		+	CD4
53 54	CPKVSFEPIPIHYCA SFEPIPIHYCAPAGF	+			CD4
62	NVSTVQCTHGIKPVV	+			CD4
104 105	ETITLPCRIKQIINM LPCRIKQIINMWQGV	+			CD8
130 131	GIVQQQSNLLRAIEA VQQSNLLRAIEAQQHL	+			CD4
134 135	AQQHLLQLTVWGIKQLQ LQLTVWGIKQLQARVL	+			CD4
Subtype B (MN)					
6223 6224	AKAYDTEVHNVWATQ DTEVHNVWATQACVP	+			CD4
6261 6262	ACPKISFEPIPIHYC ISFEPIPIHYCAPAG	+			CD4
6286 6287	RKRIHIGPGRAFYTT HIGPGRAFYTTKNII		+		CD8
6346 6347	IVQQQNNLLRAIEAQ QNNLLRAIEAQQHML	+			CD4
Subtype C (Chn19)					
4834	VPVWKEAKTTLFCASDAKSY			+	CD4
4838	GKEVHNVWATHACVPTDPNP	+		+	CD4
4848	SSENSSEYYRLINCNTSAIT	+		+	CD4
4854	STVQCTHGIKPVVSTQLLLN	+			CD4
4884	QQSNLLRAIEAQQHLLQLTV	+			CD4
4885	AQQHLLQLTVWGIKQLQTRV	+			CD4

Table 2. T cell epitope mapping of CON6.gp120 immunogen in C57BL/6 mice

Peptide	Peptide sequence	T cell response
CON 6 (consensus)		
2	GIQRNCQHLWRWGTM	CD8
3	NCQHLWRWGTMILGM	
16	DTEVHNVWATHACVP	CD4
53	CPKVSFEPIPIHYCA	CD4
97	FYCNTSGLFNSTWMF	CD8
99	FNSTWMFNGTYMFNG	CD8
Subtype B (MN)		
6210	GIRRNYQHWWGWGTM	CD8
6211	NYQHWWGWGTMLLGL	
6232	NMWKNNMVEQMHEDI	CD4
6262	ISFEPIPIHYCAPAG	CD4
6290	NIIGTIRQAHCNISR	CD4
6291	TIRQAHCNISRAKWN	
Subtype C (Chn 19)		
4830	MRVTGIRKNYQHLWRWGTML	CD8
5446	RWGTMLLGMLMICSAAEN	CD8
4836	GKEVHNVWATHACVPTDPNP	CD4
4862	GDIRQAHCNISKDKWNETLQ	CD4
4888	LLGIWGCSGKLICTTTVPWN	CD8

For the Year 2000 consensus group M *env* gene, Con-S, the Con-S envelope has been shown to be as immunogenic as the CON6 envelope gene in T cell γ interferon ELISPOT assays in two strains of mice

(the data for C57BL/6 are shown in Fig. 27). Furthermore, in comparing CON6 and Con-S gp140 Envs as protein immunogens for antibody in guinea pigs (Table 3), both gp140 Envs were found to induce antibodies that neutralized subtype B primary isolates. However, Con-S gp140 also induced robust neutralization of the subtype C isolates TV-1 and DU 123 as well as one subtype A HIV-1 primary isolate, while CON6 did not.

TABLE 3 Ability of Group M Consensus CON6 and Con-S Envs to Induce Neutralization of HIV-1 Primary Isolates

HIV-1 Isolate (Subtype)	CON6 gp140CF				CON6 gp140 CFI				CONS gp140 CFI			
	Guinea Pig Number											
	770	771	772	775	781	783	784	786	776	777	778	780
BX08(B)	520	257	428	189	218	164	>540	199	>540	>540	>540	>540
QH0692 (B)	46	55	58	77	<20	91	100	76	109	<20	<20	<20
SS1196(B)	398	306	284	222	431	242	>540	351	>540	296	>540	>540
JRLFL(B)	<20	<20	<20	<20	<20	169	<20	<20	<20	<20	<20	<20
BG1168(B)	<20	<20	<20	<20	<20	<20	<20	<20	<20	<20	<20	<20
3988(B)	<20	<20	<20	<20	<20	<20	<20	<20	<20	<20	<20	<20
6101(B)	<20	<20	<20	<20	<20	<20	<20	<20	<20	<20	<20	<20
TV-1(C)	<20	<20	<20	<20	<20	<20	<20	<20	356	439	>540	>540
DU123(C)	<20	<20	71	74	<20	72	<20	<20	176	329	387	378
DU172(C)	<20	<20	96	64	<20	<20	<20	<20	<20	235	<20	213
ZM18108.6(C)	ND	ND	ND	ND	<20	<20	<20	<20	84	61	86	43

ZM14654.7(C)	ND	ND	ND	ND	<20	<20	<20	<20	<20	<20	**30**	<20
DU151(C)	<20	<20	<20	<20	<20	<20	<20	<20	<20	<20	<20	<20
DU422(C)	<20	<20	<20	<20	<20	<20	<20	<20	<20	<20	<20	<20
DU156(C)	<20	<20	<20	<20	<20	<20	<20	<20	<20	<20	<20	<20
92RWO20(A)	<20	<20	<20	<20	<20	<20	<20	<20	**116**	**204**	**95**	**177**
92UG037(A)	<20	<20	**30**	<20	<20	**44**	<20	<20	<20	<20	<20	<20

ǂ 50% Neutralization titers after 4th or 5th immunizations

Year 2000 Con-S 140CFI.ENV sequence is shown in Fig. 26A. Gp140 CFI refers to an HIV-1 envelope design in which the cleavage-site is deleted (c), the fusion-site is deleted (F) and the gp41 immunodominant region is deleted (I), in addition to the deletion of transmembrane and cytoplasmic domains. The codon-optimized Year 2000 Con-S 140 CFI sequence is shown in Fig. 26B.

As the next iteration of consensus immunogens, and in recognition of the fact that a practical HIV-1 immunogen can be a polyvalent mixture of either several subtype consensus genes, a mixture of subtype and consensus genes, or a mixture of centralized genes and wild type genes, a series of 11 subtype consensus, and wild type genes have been designed from subtypes A, B, C, CRF AE01, and G as well as a group M consensus gene from Year 2003 Los Alamos National Database sequences. The wild type sequences were chosen either because they were known to come from early transmitted HIV-1 strains (those strains most likely to be necessary to be protected against by a vaccine) or because they were the most recently submitted strains in the database of that subtype. These nucleotide and amino acid sequences are shown in Figures 28-38 (for all 140CF designs shown, 140CF gene can be flanked with the 5' sequence "TTCAGTCGACGGCCACC" that contains a Kozak sequence (GCCACCATGG/A) and *Sal*I site and 3' sequence of TAAAGATCTTACAA containing stop codon and *Bgl*II site). Shown in Figures 39-62 are 2003 centralized (consensus and ancestral) HIV-1 envelope proteins and the codon optimized gene sequences.

Major differences between CON6 gp140 (which does not neutralize non-clade B HIV strains) and Con-S gp140 (which does induce antibodies that neutralize non-clade B HIV strains) are in Con-S V1, V2, V4 and V5 regions. For clade B strains, peptides of the V3 region can induce neutralizing

antibodies (Haynes et al, J. Immunol. 151:1646-1653 (1993)). Thus, construction of Th-V1, Th-V2, Th-V4, Th-V5 peptides can be expected to give rise to the desired broadly reactive anti-non-clade B neutralizing antibodies. Therefore, the Th-V peptides set forth in Table 4 are contemplated for use as a peptide immunogen(s) derived from Con-S gp140. The gag Th determinant (GTH, Table 4) or any homologous GTH sequence in other HIV strains, can be used to promote immunogenicity and the C4 region of HIV gp120 can be used as well (KQIINMWQVVGKAMYA) or any homologous C4 sequence from other HIV strains (Haynes et al, J. Immunol. 151:1646-1653 (1993)). Con-S V1, V2, V4, V5 peptides with an N-terminal helper determinant can be used singly or together, when formulated in a suitable adjuvant such as Corixa's RC529 (Baldridge et al, J. Endotoxin Res. 8:453-458 (2002)), to induce broadly cross reactive neutralizing antibodies to non-clade B isolates.

Table 4		
1)	GTH Con-S V1 132-150	YKRWIILGLNKIVRMYTNVNVTNTTNNTEEKGEIKN
2)	GTH Con-S V2 157-189	YKRWIILGLNKIVRMYTEIRDKKQKVYALFYRLDVVPIDDNNNNSSNYR
3)	GTH Con-S V3 294-315	YKRWIILGLNKIVRMYTRPNNNTRKSIRIGPGQAFYAT
4)	GTH Con-S V4 381-408	YKRWIILGLNKIVRMYNTSGLFNSTWIGNGTKNNNNTNDTITLP
5)	GTH Con-S V5 447-466	YKRWIILGLNKIVRMYRDGGNNNTNETEIFRPGGGD
6)	GTH Con-6 V1 132-150	YKRWIILGLNKIVRMYNVRNVSSNGTETDNEEIKN
7)	GTH Con-6 V2 157-196	YKRWIILGLNKIVRMYTELRDKKQKVYALFYRLDVVPIDDKNSSEISGKNSSEYYR
8)	GTH-Con6 V3 301-322	YKRWIILGLNKIVRMYTRPNNNTRKSIHIGPGQAFYAT
9)	GTH Con-6 V4 388-418	YKRWIILGLNKIVRMYNTSGLFNSTWMFNGTYMFNGTKDNSETITLP
10	GTH Con 6 V5 457-477	YKRWIILGLNKIVRMYRDGGNNSNKNKTETFRPGGGD

It will be appreciated that the invention includes portions and variants of the sequences specifically disclosed herein. For example, forms of codon optimized consensus encoding sequences can be constructed as gp140CF, gp140 CFI, gp120 or gp160 forms with either gp120/41 cleaved or uncleaved. For example, and as regards the consensus and ancestral envelope sequences, the invention encompasses envelope sequences devoid of V3. Alternatively, V3 sequences can be selected from preferred sequences, for example, those described in U.S. Application No. 10/431,596 and U.S. Provisional Application No. 60/471,327. In addition, an optimal immunogen for breadth of response can include mixtures of group M consensus *gag*, *pol*, *nef* and *env* encoding sequences, and as well as consist of

mixtures of subtype consensus or ancestral encoding sequences for *gag*, *pol*, *nef* and *env* HIV genes. For dealing with regional differences in virus strains, an efficacious mixture can include mixtures of consensus/ancestral and wild type encoding sequences.

A consensus or ancestral envelope of the invention can be been "activated" to expose intermediate conformations of neutralization epitopes that normally are only transiently or less well exposed on the surface of the HIV virion. The immunogen can be a "frozen" triggered form of a consensus or ancestral envelope that makes available specific epitopes for presentation to B lymphocytes. The result of this epitope presentation is the production of antibodies that broadly neutralize HIV. (Attention is directed to WO 02/024149 and to the activated/triggered envelopes described therein.)

The concept of a fusion intermediate immunogen is consistent with observations that the gp41 HR-2 region peptide, DP178, can capture an uncoiled conformation of gp41 (Furata et al, Nature Struct. Biol. 5:276 (1998)), and that formalin-fixed HIV-infected cells can generate broadly neutralizing antibodies (LaCasse et al, Science 283:357 (1997)). Recently a monoclonal antibody against the coiled-coil region bound to a conformational determinant of gp41 in HR1 and HR2 regions of the coiled-coil gp41 structure, but did not neutralize HIV (Jiang et al, J. Virol. 10213 (1998)). However, this latter study

proved that the coiled-coil region is available for antibody to bind if the correct antibody is generated.

The immunogen of one aspect of the invention comprises a consensus or ancestral envelope either in soluble form or anchored, for example, in cell vesicles or in liposomes containing translipid bilayer envelope. To make a more native envelope, gp140 or gp160 consensus or ancestral sequences can be configured in lipid bilayers for native trimeric envelope formation. Alternatively, triggered gp160 in aldrithio 1-2 inactivated HIV-1 virions can be used as an immunogen. The gp160 can also exist as a recombinant protein either as gp160 or gp140 (gp140 is gp160 with the transmembrane region and possibly other gp41 regions deleted). Bound to gp160 or gp140 can be recombinant CCR5 or CXCR4 co-receptor proteins (or their extracellular domain peptide or protein fragments) or antibodies or other ligands that bind to the CXCR4 or CCR5 binding site on gp120, and/or soluble CD4, or antibodies or other ligands that mimic the binding actions of CD4. Alternatively, vesicles or liposomes containing CD4, CCR5 (or CXCR4), or soluble CD4 and peptides reflective of CCR5 or CXCR4 gp120 binding sites. Alternatively, an optimal CCR5 peptide ligand can be a peptide from the N-terminus of CCR5 wherein specific tyrosines are sulfated (Bormier et al, Proc. Natl. Acad. Sci. USA 97:5762 (2001)). The triggered immunogen may not need to be bound to a membrane but may exist and be triggered in solution.

Alternatively, soluble CD4 (sCD4) can be replaced by an envelope (gp140 or gp160) triggered by CD4 peptide mimetopes (Vitra et al, Proc. Natl. Acad. Sci. USA 96:1301 (1999)). Other HIV co-receptor molecules that "trigger" the gp160 or gp140 to undergo changes associated with a structure of gp160 that induces cell fusion can also be used. Ligation of soluble HIV gp140 primary isolate HIV 89.6 envelope with soluble CD4 (sCD4) induced conformational changes in gp41.

In one embodiment, the invention relates to an immunogen that has the characteristics of a receptor (CD4)-ligated consensus or ancestral envelope with CCR5 binding region exposed but unlike CD4-ligated proteins that have the CD4 binding site blocked, this immunogen has the CD4 binding site exposed (open). Moreover, this immunogen can be devoid of host CD4, which avoids the production of potentially harmful anti-CD4 antibodies upon administration to a host.

The immunogen can comprise consensus or ancestral envelope ligated with a ligand that binds to a site on gp120 recognized by an A32 monoclonal antibodies (mab) (Wyatt et al, J. Virol. 69:5723 (1995), Boots et al, AIDS Res. Hum. Retro. 13:1549 (1997), Moore et al, J. Virol. 68:8350 (1994), Sullivan et al, J. Virol. 72:4694 (1998), Fouts et al, J. Virol. 71:2779 (1997), Ye et al, J. Virol. 74:11955 (2000)). One A32 mab has been shown to mimic CD4 and when bound to gp120, upregulates (exposes) the CCR5 binding site (Wyatt et al, J.

Virol. 69:5723 (1995)). Ligation of gp120 with such a ligand also upregulates the CD4 binding site and does not block CD4 binding to gp120. Advantageously, such ligands also upregulate the HR-2 binding site of gp41 bound to cleaved gp120, uncleaved gp140 and cleaved gp41, thereby further exposing HR-2 binding sites on these proteins - each of which are potential targets for anti-HIV neutralizing antibodies.

In a specific aspect of this embodiment, the immunogen comprises soluble HIV consensus or ancestral gp120 envelope ligated with either an intact A32 mab, a Fab2 fragment of an A32 mab, or a Fab fragment of an A32 mab, with the result that the CD4 binding site, the CCR5 binding site and the HR-2 binding site on the consensus or ancestral envelope are exposed/upregulated. The immunogen can comprise consensus or ancestral envelope with an A32 mab (or fragment thereof) bound or can comprise consensus or ancestral envelope with an A32 mab (or fragment thereof) bound and cross-linked with a cross-linker such as .3% formaldehyde or a heterobifunctional cross-linker such as DTSSP (Pierce Chemical Company). The immunogen can also comprise uncleaved consensus or ancestral gp140 or a mixture of uncleaved gp140, cleaved gp41 and cleaved gp120. An A32 mab (or fragment thereof) bound to consensus or ancestral gp140 and/or gp120 or to gp120 non-covalently bound to gp41, results in upregulation (exposure) of HR-2 binding sites in gp41, gp120 and uncleaved gp140. Binding of an A32 mab (or fragment

thereof) to gp120 or gp140 also results in upregulation of the CD4 binding site and the CCR5 binding site. As with gp120 containing complexes, complexes comprising uncleaved gp140 and an A32 mab (or fragment thereof) can be used as an immunogen uncross-linked or cross-linked with cross-linker such as .3% formaldehyde or DTSSP. In one embodiment, the invention relates to an immunogen comprising soluble uncleaved consensus or ancestral gp140 bound and cross linked to a Fab fragment or whole A32 mab, optionally bound and cross-linked to an HR-2 binding protein.

The consensus or ancestral envelope protein triggered with a ligand that binds to the A32 mab binding site on gp120 can be administered in combination with at least a second immunogen comprising a second envelope, triggered by a ligand that binds to a site distinct from the A32 mab binding site, such as the CCR5 binding site recognized by mab 17b. The 17b mab (Kwong et al, Nature 393:648 (1998) available from the AIDS Reference Repository, NIAID, NIH) augments sCD4 binding to gp120. This second immunogen (which can also be used alone or in combination with triggered immunogens other than that described above) can, for example, comprise soluble HIV consensus or ancestral envelope ligated with either the whole 17b mab, a Fab2 fragment of the 17b mab, or a Fab fragment of the 17b mab. It will be appreciated that other CCR5 ligands, including other antibodies (or fragments thereof), that result in the CD4 binding site being

exposed can be used in lieu of the 17b mab. This further immunogen can comprise gp120 with the 17b mab, or fragment thereof, (or other CCR5 ligand as indicated above) bound or can comprise gp120 with the 17b mab, or fragment thereof, (or other CCR5 ligand as indicated above) bound and cross-linked with an agent such as .3% formaldehyde or a heterobifunctional cross-linker, such as DTSSP (Pierce Chemical Company). Alternatively, this further immunogen can comprise uncleaved gp140 present alone or in a mixture of cleaved gp41 and cleaved gp120. Mab 17b, or fragment thereof (or other CCR5 ligand as indicated above) bound to gp140 and/or gp120 in such a mixture results in exposure of the CD4 binding region. The 17b mab, or fragment thereof, (or other CCR5 ligand as indicated above) gp140 complexes can be present uncross-linked or cross-linked with an agent such as .3% formaldehyde or DTSSP.

Soluble HR-2 peptides, such as T649Q26L and DP178, can be added to the above-described complexes to stabilize epitopes on consensus gp120 and gp41 as well as uncleaved consensus gp140 molecules, and can be administered either cross-linked or uncross-linked with the complex.

A series of monoclonal antibodies (mabs) have been made that neutralize many HIV primary isolates, including, in addition to the 17b mab described above, mab IgG1b12 that binds to the CD4 binding site on gp120(Roben et al, J. Virol. 68:482 (1994), Mo et al, J. Virol. 71:6869 (1997)), mab 2G12 that

binds to a conformational determinant on gp120 (Trkola et al, J. Virol. 70:1100 (1996)), and mab 2F5 that binds to a membrane proximal region of gp41 (Muster et al, J. Virol. 68:4031 (1994)).

As indicated above, various approaches can be used to "freeze" fusogenic epitopes in accordance with the invention. For example, "freezing" can be effected by addition of the DP-178 or T-649Q26L peptides that represent portions of the coiled coil region, and that when added to CD4-triggered consensus or ancestral envelope, result in prevention of fusion (Rimsky et al, J. Virol. 72:986-993 (1998)). HR-2 peptide bound consensus or ancestral gp120, gp140, gp41 or gp160 can be used as an immunogen or crosslinked by a reagent such as DTSSP or DSP (Pierce Co.), formaldehyde or other crosslinking agent that has a similar effect.

"Freezing" can also be effected by the addition of 0.1% to 3% formaldehyde or paraformaldehyde, both protein cross-linking agents, to the complex, to stabilize the CD4, CCR5 or CXCR4, HR-2 peptide gp160 complex, or to stabilize the "triggered" gp41 molecule, or both (LaCasse et al, Science 283:357-362 (1999)).

Further, "freezing" of consensus or ancestral gp41 or gp120 fusion intermediates can be effected by addition of heterobifunctional agents such as DSP (dithiobis[succimidylproprionate]) (Pierce Co. Rockford, ILL., No. 22585ZZ) or the water soluble DTSSP (Pierce Co.) that use two NHS esters that are reactive with amino groups to cross link and

stabilize the CD4, CCR5 or CXCR4, HR-2 peptide gp160 complex, or to stabilize the "triggered" gp41 molecule, or both.

Analysis of T cell immune responses in immunized or vaccinated animals and humans shows that the envelope protein is normally not a main target for T cell immune response although it is the only gene that induces neutralizing antibodies. HIV-1 Gag, Pol and Nef proteins induce a potent T cell immune response. Accordingly, the invention includes a repertoire of consensus or ancestral immunogens that can induce both humoral and cellular immune responses. Subunits of consensus or ancestral sequences can be used as T or B cell immunogens. (See Examples 6 and 7, and Figures referenced therein, and Figures 63-127.

The immunogen of the invention can be formulated with a pharmaceutically acceptable carrier and/or adjuvant (such as alum) using techniques well known in the art. Suitable routes of administration of the present immunogen include systemic (e.g. intramuscular or subcutaneous). Alternative routes can be used when an immune response is sought in a mucosal immune system (e.g., intranasal).

The immunogens of the invention can be chemically synthesized and purified using methods which are well known to the ordinarily skilled artisan. The immunogens can also be synthesized by well-known recombinant DNA techniques. Nucleic acids encoding the immunogens of the invention can

be used as components of, for example, a DNA vaccine wherein the encoding sequence is administered as naked DNA or, for example, a minigene encoding the immunogen can be present in a viral vector. The encoding sequence can be present, for example, in a replicating or non-replicating adenoviral vector, an adeno-associated virus vector, an attenuated mycobacterium tuberculosis vector, a Bacillus Calmette Guerin (BCG) vector, a vaccinia or Modified Vaccinia Ankara (MVA) vector, another pox virus vector, recombinant polio and other enteric virus vector, Salmonella species bacterial vector, Shigella species bacterial vector, Venezuelean Equine Encephalitis Virus (VEE) vector, a Semliki Forest Virus vector, or a Tobacco Mosaic Virus vector. The encoding sequence, can also be expressed as a DNA plasmid with, for example, an active promoter such as a CMV promoter. Other live vectors can also be used to express the sequences of the invention. Expression of the immunogen of the invention can be induced in a patient's own cells, by introduction into those cells of nucleic acids that encode the immunogen, preferably using codons and promoters that optimize expression in human cells. Examples of methods of making and using DNA vaccines are disclosed in U.S. Pat. Nos. 5,580,859, 5,589,466, and 5,703,055.

The composition of the invention comprises an immunologically effective amount of the immunogen of this invention, or nucleic acid sequence encoding same, in a pharmaceutically acceptable delivery

system. The compositions can be used for prevention and/or treatment of immunodeficiency virus infection. The compositions of the invention can be formulated using adjuvants, emulsifiers, pharmaceutically-acceptable carriers or other ingredients routinely provided in vaccine compositions. Optimum formulations can be readily designed by one of ordinary skill in the art and can include formulations for immediate release and/or for sustained release, and for induction of systemic immunity and/or induction of localized mucosal immunity (e.g, the formulation can be designed for intranasal administration). The present compositions can be administered by any convenient route including subcutaneous, intranasal, oral, intramuscular, or other parenteral or enteral route. The immunogens can be administered as a single dose or multiple doses. Optimum immunization schedules can be readily determined by the ordinarily skilled artisan and can vary with the patient, the composition and the effect sought.

The invention contemplates the direct use of both the immunogen of the invention and/or nucleic acids encoding same and/or the immunogen expressed as minigenes in the vectors indicated above. For example, a minigene encoding the immunogen can be used as a prime and/or boost.

Certain aspects of the invention can be described in greater detail in the non-limiting Examples that follows.

EXAMPLE 1

Artificial HIV-1 Group M Consensus Envelope

EXPERIMENTAL DETAILS

Expression of CON6 gp120 and gp140 proteins in recombinant vaccinia viruses (VV). To express and purify the secreted form of HIV-1 CON6 envelope proteins, CON6 gp120 and gp140CF plasmids were constructed by introducing stop codons after the gp120 cleavage site (REKR) and before the transmembrane domain (YIKIFIMIVGGLIGLRIVFAVLSIVN), respectively. The gp120/gp41 cleavage site and fusion domain of gp41 were deleted in the gp140CF protein. Both CON6 gp120 and gp140CF DNA constructs were cloned into the pSC65 vector (from Bernard Moss, NIH, Bethesda, MD) at SalI and KpnI restriction enzyme sites. This vector contains the lacZ gene that is controlled by the p7.5 promoter. A back-to-back P E/L promoter was used to express CON6 *env* genes. BSC-1 cells were seeded at 2×10^5 in each well in a 6-well plate, infected with wild-type vaccinia virus (WR) at a MOI of 0.1 pfu/cell, and 2 hr after infection, pSC65-derived plasmids containing CON6 *env* genes were transfected into the VV-infected cells and recombinant (r) VV selected as described (Moss and Earl, Current Protocols in Molecular Biology, eds, Ausubel et al (John Wiley & Sons, Inc. Indianapolis, IN) pp. 16.15.1-16.19.9 (1998)). Recombinant VV that contained the CON6 *env*

genes were confirmed by PCR and sequencing analysis. Expression of the CON6 envelope proteins was confirmed by SDS-PAGE and Western blot assay. Recombinant CON6 gp120 and gp140CF were purified with agarose *galanthus Nivalis* lectin beads (Vector Labs, Burlingame, CA), and stored at -70°C until use. Recombinant VV expressing JRFL (vCB-28) or 96ZM651 (vT241R) gp160 were obtained from the NIH AIDS Research and Reference Reagent Program (Bethesda, MD).

Monoclonal Antibodies and gp120 Wild-type Envelopes. Human mabs against a conformational determinant on gp120 (A32), the gp120 V3 loop (F39F) and the CCR5 binding site (17b) were the gifts of James Robinson (Tulane Medical School, New Orleans, LA) (Wyatt et al, Nature 393;705-711 (1998), Wyatt et al, J. Virol. 69:5723-5733 (1995)). Mabs 2F5, 447, b12, 2G12 and soluable CD4 were obtained from the NIH AIDS Research and Reference Reagent Program (Bethesda, MD) (Gorny et al, J. Immunol. 159:5114-5122 (1997), Nyambi et al, J. Virol. 70:6235-6243 (1996), Purtscher et al, AIDS Res. Hum. Retroviruses 10:1651-1658 (1994), Trkola et al, J. Virol 70:1100-1108 (1996)). T8 is a murine mab that maps to the gp120 C1 region (a gift from P. Earl, NIH, Bethesda, MD). BaL (subtype B), 96ZM651 (subtype C), and 93TH975 (subtype E) gp120s were provided by QBI, Inc. and the Division of AIDS, NIH. CHO cell lines that express 92U037 (subtype A) and 93BR029 (subtype

F) gp140 (secreted and uncleaved) were obtained from NICBS, England.

Surface Plasmon Resonance Biosensor (SPR) Measurements and ELISA. SPR biosensor measurements were determined on a BIAcore 3000 instrument (BIAcore Inc., Uppsala, Sweden) instrument and data analysis was performed using BIAevaluation 3.0 software (BIAcore Inc, Upsaala, Sweden). Anti-gp120 mabs (T8, A32, 17b, 2G12) or sCD4 in 10mM Na-acetate buffer, pH 4.5 were directly immobilized to a CM5 sensor chip using a standard amine coupling protocol for protein immobilization. FPLC purified CON6 gp120 monomer or gp140CF oligomer recombinant proteins were flowed over CM5 sensor chips at concentrations of 100 and 300 μg/ml, respectively. A blank in-line reference surface (activated and de-activated for amine coupling) or non-bonding mab controls were used to subtract non-specific or bulk responses. Soluble 89.6 gp120 and irrelevant IgG was used as a positive and negative control respectively and to ensure activity of each mab surface prior to injecting the CON6 Env proteins. Binding of CON6 envelope proteins was monitored in real-time at 25°C with a continuous flow of PBS (150 mM NaCl, 0.005% surfactant P20), pH 7.4 at 10-30 μl/min. Bound proteins were removed and the sensor surfaces were regenerated following each cycle of binding by single or duplicate 5-10 μl pulses of regeneration solution (10 mM glycine-HCl, pH 2.9).

ELISA was performed to determine the reactivity of various mabs to CON6 gp120 and gp140CF proteins as described (Haynes et al, AIDS Res. Hum. Retroviruses 11:211-221 (1995)). For assay of human mab binding to rgp120 or gp140 proteins, end-point titers were defined as the highest titer of mab (beginning at 20 μg/ml) at which the mab bound CON6 gp120 and gp140CF Env proteins ≥ 3 fold over background control (non-binding human mab).

Infectivity and coreceptor usage assays. HIV-1/SG3Δenv and CON6 or control *env* plasmids were cotransfected into human 293T cells. Pseudotyped viruses were harvested, filtered and p24 concentration was quantitated (DuPont/NEN Life Sciences, Boston, MA). Equal amounts of p24 (5 ng) for each pseudovirion were used to infect JC53-BL cells to determine the infectivity (Derdeyn e al, J. Virol. 74:8358-8367 (2000), Wei et al, Antimicrob Agents Chemother. 46:1896-1905 (2002)). JC53-BL cells express CD4, CCR5 and CXCR4 receptors and contain a β-galactosidase (β-gal) gene stably integrated under the transcriptional control of an HIV-1 long terminal repeat (LTR). These cells can be used to quantify the infectious titers of pseudovirion stocks by staining for β-gal expression and counting the number of blue cells (infectious units) per microgram of p24 of pseudovirons (IU/μg p24) (Derdeyn e al, J. Virol. 74:8358-8367 (2000), Wei et al, Antimicrob Agents Chemother. 46:1896-1905

(2002)). To determine the coreceptor usage of the CON6 *env* gene, JC53BL cells were treated with 1.2 μM AMD3100 and 4 μM TAK-799 for 1 hr at 37°C then infected with equal amounts of p24 (5 ng) of each Env pseudotyped virus. The blockage efficiency was expressed as the percentage of the infectious units from blockage experiments compared to that from control culture without blocking agents. The infectivity from control group (no blocking agent) was arbitrarily set as 100%.

Immunizations. All animals were housed in the Duke University Animal Facility under AALAC guidelines with animal use protocols approved by the Duke University Animal Use and Care Committee. Recombinant CON6 gp120 and gp140CF glycoproteins were formulated in a stable emulsion with RIBI-CWS adjuvant based on the protocol provided by the manufacturer (Sigma Chemical Co., St. Louis, MO). For induction of anti-envelope antibodies, each of four out-bred guinea pigs (Harlan Sprague, Inc., Chicago, IL) was given 100 μg either purified CON6 gp120 or gp140CF subcutaneously every 3 weeks (total of 5 immunizations). Serum samples were heat-inactivated (56°C, 1 hr), and stored at -20°C until use.

For induction of anti-envelope T cell responses, 6-8 wk old female BALB/c mice (Frederick Cancer Research and Developmental Center, NCI, Frederick, MD) were immunized i.m. in the quadriceps

with 50 μg plasmid DNA three times at a 3-week interval. Three weeks after the last DNA immunization, mice were boosted with 10^7 PFU of rVV expressing Env proteins. Two weeks after the boost, all mice were euthanized and spleens were removed for isolation of splenocytes.

Neutralization assays. Neutralization assays were performed using either a MT-2 assay as described in Bures et al, AIDS Res. Hum. Retroviruses 16:2019-2035 (2000), a luciferase-based multiple replication cycle HIV-1 infectivity assay in 5.25.GFP.Luc.M7 cells using a panel of HIV-1 primary isolates (Bures et al, AIDS Res. Hum. Retroviruses 16:2019-2035 (2000), Bures et al, J. Virol. 76:2233-2244 (2002)), or a syncytium (fusion from without) inhibition assay using inactivated HIV-1 virions (Rossio et al, J. Virol. 72:7992-8001 (1998)). In the luciferase-based assay, neutralizing antibodies were measured as a function of a reduction in luciferase acitivity in 5.25.EGFP.Luc.M7 cells provided by Nathaniel R. Landau, Salk Institute, La Jolla, CA (Brandt et al, J. Biol. Chem. 277:17291-17299 (2002)). Five hundred tissue culture infectious dose 50 ($TCID_{50}$) of cell-free virus was incubated with indicated serum dilutions in 150 μl (1 hr, at 37°C) in triplicate in 96-well flat-bottom culture plates. The 5.25.EGFP.Luc.M7 cells were suspended at a density of 5 x 10^5/ml in media containing DEAE dextran (10

µg/ml). Cells (100 µl) were added and until 10% of cells in control wells (no test serum sample) were positive for GFP expression by fluorescence microscopy. At this time the cells were concentrated 2-fold by removing one-half volume of media. A 50 µl suspension of cells was transferred to 96-well white solid plates (Costar, Cambridge, MA) for measurement of luciferase activity using Bright-Glo™ substrate (Promega, Madison, WI) on a Wallac 1420 Multilabel Counter (PerkinElmer Life Sciences, Boston, MA). Neutralization titers in the MT-2 and luciferase assays were those where $\geq$ 50% virus infection was inhibited. Only values that titered beyond 1:20 (i.e. >1:30) were considered significantly positive. The syncytium inhibition "fusion from without" assay utilized HIV-1 aldrithiol-2 (AT-2) inactivated virions from HIV-1 subtype B strains ADA and AD8 (the gift of Larry Arthur and Jeffrey Lifson, Frederick Research Cancer Facility, Frederick, MD) added to SupT1 cells, with syncytium inhibition titers determined as those titers where $\geq$90% of syncytia were inhibited compared to prebleed sera.

Enzyme linked immune spot (ELISPOT) assay. Single-cell suspensions of splenocytes from individual immunized mice were prepared by mincing and forcing through a 70 µm Nylon cell strainer (BD Labware, Franklin Lakes, NJ). Overlapping Env peptides of CON6 gp140 (159 peptides, 15mers

overlapping by 11) were purchased from Boston Bioscence, Inc (Royal Oak, MI). Overlapping Env peptides of MN gp140 (subtype B; 170 peptides, 15mers overlapping by 11) and Chn19 gp140 (subtype C; 69 peptides, 20mers overlapping by 10) were obtained from the NIH AIDS Research and Reference Reagent Program (Bethesda, MD). Splenocytes (5 mice/group) from each mouse were stimulated *in vitro* with overlapping Env peptides pools from CON6, subtype B and subtype C Env proteins. 96-well PVDF plates (MultiScreen-IP, Millipore, Billerica, MA) were coated with anti-IFN-γ mab (5 μg/ml, AN18; Mabtech, Stockholm, Sweden). After the plates were blocked at 37°C for 2 hr using complete Hepes buffered RPMI medium, 50μl of the pooled overlapping envelope peptides (13 CON6 and MN pools, 13-14 peptides in each pool; 9 Chn19 pool, 7-8 peptide in each pool) at a final concentration of 5 μg/ml of each were added to the plate. Then 50 μl of splenocytes at a concentration of 1.0 X 10^7/ml were added to the wells in duplicate and incubated for 16 hr at 37°C with 5% CO_2. The plates were incubated with 100 μl of a 1:1000 dilution of streptavidin alkaline phosphatase (Mabtech, Stockholm, Sweden), and purple spots developed using 100 μl of BCIP/NBT (Plus) Alkaline Phosphatase Substrate (Moss, Pasadena, MD). Spot forming cells (SFC) were measured using an Immunospot counting system (CTL Analyzers, Cleveland, OH). Total responses for each

envelope peptide pool are expressed as SFCs per 10^6 splenocytes.

RESULTS

CON6 Envelope Gene Design, Construction and Expression. An artificial group M consensus *env* gene (CON6) was constructed by generating consensus sequences of *env* genes for each HIV-1 subtype from sequences in the Los Alamos HIV Sequence Database, and then generating a consensus sequence of all subtype consensuses to avoid heavily sequenced subtypes (Gaschen et al, Science 296:2354-2360 (2002), Korber et al, Science 288:1789-1796 (2000)). Five highly variable regions from a CRF08_BC recombinant strain (98CN006) (V1, V2, V4, V5 and a region in cytoplasmic domain of gp41) were then used to fill in the missing regions in CON6 sequence. The CON6 V3 region is group M consensus (Figure 1A). For high levels of expression, the codons of CON6 *env* gene were optimized based on codon usage for highly expressed human genes (Haas et al, Curr. Biol. 6:315-324 (2000), Andre et al, J. Virol. 72:1497-1503 (1998)). (See Fig. 1D.) The codon optimized CON6 env gene was constructed and subcloned into pcDNA3.1 DNA at EcoR I and BamH I sites (Gao et al, AIDS Res. Hum. Retroviruses, 19:817-823 (2003)). High levels of protein expression were confirmed with Western-blot assays after transfection into 293T cells. To obtain recombinant CON6 Env proteins for characterization

and use as immunogens, rVV was generated to express secreted gp120 and uncleaved gp140CF (Figure 1B). Purity for each protein was ≥90% as determined by Coomassie blue gels under reducing conditions (Figure 1C).

CD4 Binding Domain and Other Wild-type HIV-1 Epitopes are Preserved on CON6 Proteins. To determine if CON6 proteins can bind to CD4 and express other wild-type HIV-1 epitopes, the ability of CON6 gp120 and gp140CF to bind soluble(s) CD4, to bind several well-characterized anti-gp120 mabs, and to undergo CD4-induced conformational changes was assayed. First, BIAcore CM5 sensor chips were coated with either sCD4 or mabs to monitor their binding activity to CON6 Env proteins. It was found that both monomeric CON6 gp120 and oligomeric gp140CF efficiently bound sCD4 and anti-gp120 mabs T8, 2G12 and A32, but did not constitutively bind mab 17b, that recognizes a CD4 inducible epitope in the CCR5 binding site of gp120 (Figures 2A and 2B). Both sCD4 and A32 can expose the 17b binding epitope after binding to wild-type gp120 (Wyatt et al, Nature 393;705-711 (1998), Wyatt et al, J. Virol. 69:5723-5733 (1995)). To determine if the 17b epitope could be induced on CON6 Envs by either sCD4 or A32, sCD4, A32 and T8 were coated on sensor chips, then CON6 gp120 or gp140CF captured, and mab 17b binding activity monitored. After binding sCD4 or mab A32, both CON6 gp120 and gp140CF were triggered to undergo conformational changes and

bound mab 17b (Figures 2C and 2D). In contrast, after binding mab T8, the 17b epitope was not exposed (Figures 2C and 2D). ELISA was next used to determine the reactivity of a panel of human mabs against the gp120 V3 loop (447, F39F), the CD4 binding site (b12), and the gp41 neutralizing determinant (2F5) to CON6 gp120 and gp140CF (Figure 2E). Both CON6 rgp120 and rgp140CF proteins bound well to neutralizing V3 mabs 447 and F39F and to the potent neutralizing CD4 binding site mab b12. Mab 2F5, that neutralizes HIV-1 primary isolates by binding to a C-terminal gp41 epitope, also bound well to CON6 gp140CF (Figure 2E).

CON6 env Gene is Biologically Functional and Uses CCR5 as its Coreceptor. To determine whether CON6 envelope gene is biologically functional, it was co-transfected with the *env*-defective SG3 proviral clone into 293T cells. The pseudotyped viruses were harvested and JC53BL cells infected. Blue cells were detected in JC53-BL cells infected with the CON6 Env pseudovirions, suggesting that CON6 Env protein is biologically functional (Figure 3A). However, the infectious titers were 1-2 logs lower than that of pseudovirions with either YU2 or NL4-3 wild-type HIV-1 envelopes.

The co-receptor usage for the CON6 *env* gene was next determined. When treated with CXCR4 blocking agent AMD3100, the infectivity of NL4-3 Env-pseudovirons was blocked while the infectivity of YU2 or CON6 Env-pseudovirons was not inhibited

(Figure 3B). In contrast, when treated with CCR5 blocking agent TAK-779, the infectivity of NL4-3 Env-pseudovirons was not affected, while the infectivity of YU2 or CON6 Env-pseudovirons was inhibited. When treated with both blocking agents, the infectivity of all pseudovirions was inhibited. Taken together, these data show that the CON6 envelope uses the CCR5 co-receptor for its entry into target cells.

Reaction of CON6 gp120 With Different Subtype Sera. To determine if multiple subtype linear epitopes are preserved on CON6 gp120, a recombinant Env protein panel (gp120 and gp140) was generated. Equal amounts of each Env protein (100 ng) were loaded on SDS-polyacrylamide gels, transferred to nitrocellulose, and reacted with subtype A through G patient sera as well as anti-CON6 gp120 guinea pig sera (1:1,000 dilution) in Western blot assays. For each HIV-1 subtype, four to six patient sera were tested. One serum representative for each subtype is shown in Figure 4.

It was found that whereas all subtype sera tested showed variable reactivities among Envs in the panel, all group M subtype patient sera reacted equally well with CON6 gp120 Env protein, demonstrating that wild-type HIV-1 Env epitopes recognized by patient sera were well preserved on the CON6 Env protein. A test was next made as to whether CON6 gp120 antiserum raised in guinea pigs could react to different subtype Env proteins. It

was found that the CON6 serum reacted to its own and other subtype Env proteins equally well, with the exception of subtype A Env protein (Figure 4).

Induction of T Cell Responses to CON6, Subtype B and Subtype C Envelope Overlapping Peptides. To compare T cell immune responses induced by CON6 Env immunogens with those induced by subtype specific immunogens, two additional groups of mice were immunized with subtype B or subtype C DNAs and with corresponding rVV expressing subtype B or C envelope proteins. Mice immunized with subtype B (JRFL) or subtype C (96ZM651) Env immunogen had primarily subtype-specific T cell immune responses (Figure 5). IFN-γ SFCs from mice immunized with JRFL (subtype B) immunogen were detected after stimulation with subtype B (MN) peptide pools, but not with either subtype C (Chn19) or CON6 peptide pools. IFN-γ SFCs from mice immunized with 96ZM651 (subtype C) immunogen were detected after the stimulation with both subtype C (Chn19) and CON6 peptide pools, but not with subtype B (MN) peptide pools. In contrast, IFN-γ SFCs were identified from mice immunized with CON6 Env immunogens when stimulated with either CON6 peptide pools as well as by subtype B or C peptide pools (Figure 5). The T cell immune responses induced by CON6 gp140 appeared more robust than those induced by CON6 gp120. Taken together, these data demonstrated that CON6 gp120 and gp140CF immunogens were capable of inducing T cell responses

that recognized T cell epitopes of wild-type subtype B and C envelopes.

Induction of Antibodies by Recombinant CON6 gp120 and gp140CF Envelopes that Neutralize HIV-1 Subtype B and C Primary Isolates. To determine if the CON6 envelope immunogens can induce antibodies that neutralize HIV-1 primary isolates, guinea pigs were immunized with either CON6 gp120 or gp140CF protein. Sera collected after 4 or 5 immunizations were used for neutralization assays and compared to the corresponding prebleed sera. Two AT-2 inactivated HIV-1 isolates (ADA and AD8) were tested in syncytium inhibition assays (Table 5A). Two subtype B SHIV isolates, eight subtype B primary isolates, four subtype C, and one each subtype A, D, and E primary isolates were tested in either the MT-2 or the luciferase-based assay (Table 5B). In the syncytium inhibition assay, it was found that antibodies induced by both CON 6 gp120 and gp140CF proteins strongly inhibited AT-2 inactivated ADA and AD8-induced syncytia (Table 5A). In the MT-2 assay, weak neutralization of 1 of 2 SHIV isolates (SHIV SF162P3) by two gp120 and one gp140CF sera was found (Table 5B). In the luciferase-based assay, strong neutralization of 4 of 8 subtype B primary isolates (BXO8, SF162, SS1196, and BAL) by all gp120 and gp140CF sera was found, and weak neutralization of 2 of 8 subtype B isolates (6101, 0692) by most gp120 and gp140CF sera was found. No neutralization was detected against HIV-1 PAVO (Table 5B). Next, the

CON6 anti-gp120 and gp140CF sera were tested against four subtype C HIV-1 isolates, and weak neutralization of 3 of 4 isolates (DU179, DU368, and S080) was found, primarily by anti-CON6 gp120 sera. One gp140CF serum, no. 653, strongly neutralized DU179 and weakly neutralized S080 (Table 5B). Finally, anti-CON6 Env sera strongly neutralized a subtype D isolate (93ZR001), weakly neutralized a subtype E (CM244) isolate, and did not neutralize a subtype A (92RW020) isolate.

Table 5A

Ability of HIV-1 Group M Consensus Envelope CON6 Proteins to Induce Fusion Inhibiting Antibodies

Guinea Pig No.	Immunogen	Syncytium Inhibition antibody titer[1] AD8	ADA
646	gp120	270	270
647	gp120	90	90
648	gp120	90	270
649	gp120	90	90
Geometric Mean Titer		119	156
650	gp140	270	270
651	gp140	90	90
652	gp140	≥810	810
653	gp140	270	90
Geometric Mean Titer		270	207

[1]Reciprocal serum dilution at which HIV-induced syncytia of Sup T1 cells was inhibited by >90% compared to pre-immune serum. All prebleed sera were negative (titer <10).

Table 5B

Ability of Group M Consensus HIV-1 Envelope CON6 gp120 and gp140CF Proteins to Induce Antibodies that Neutralize HIV Primary Isolates

HIV Isolate (Subtype)	CON6 gp120 Protein Guinea Pig No.					CON6 gp140CF Protein Guinea Pig No.					Controls		
	646	647	648	649	GMT	650	651	652	653	GMT	TriMab‡	CD4-IgG2	HIV+ Serum
SHIV 89.6P*(B)	<20	<20	<20	<20	<20	<20	<20	<20	<20	<20	NT	NT	NT
SHIV SF162P3*(B)	<20	30	48	<20	<20	27	<20	<20	<20	<20	NT	0.2µg/ml	NT
BX08(B)	270	183	254	55	102	199	64	229	150	187	0.7µg/ml	NT	2384
6101(B)	<20	38	35	<20	<20	<20	90	72	73	39	1.1µg/ml	NT	NT
BG1168(B)	<20	<20	<20	<20	<20	40	<20	<20	25	<20	2.7µg/ml	NT	NT
0692(B)	31	32	34	<20	24	28	33	30	45	33	0.8µg/ml	NT	769
PAVO(B)	<20	<20	<20	<20	<20	<20	<20	<20	<20	<20	2.9µg/ml	NT	NT
SF162(B)	2,146	308	110	282	379	206	5,502	15,098	174	1,313	NT	NT	>540
SS1196(B)	206	26	148	59	83	381	401	333	81	253	NT	NT	301#
BAL(B)	123	90	107	138	113	107	146	136	85	116	NT	NT	3307
92RW020(A)	<20	<20	<20	<20	<20	<20	<20	<20	<20	<20	NT	NT	693
DU179(C)	<20	43	<20	24	<20	<20	<20	24	515	33	NT	0.8µg/ml	NT
DU368(C)	25	35	62	<20	27	<20	<20	<20	23	<20	NT	2.3µg/ml	NT
S021(C)	<20	<20	33	<20	<20	<20	<20	<20	<20	<20	NT	8.3µg/ml	NT
S080(C)	24	37	70	41	40	<20	<20	<20	52	<20	NT	3.4µg/ml	NT
93ZR001(D)	275	144	126	114	154	306	195	129	173	191	NT	NT	693
CM244(E)	35	43	64	ND	46	31	25	27	25	26	NT	NT	693

*MT-2 Assay; All other HIV isolates were tested in the M7-luciferase assay.

HIV-1 isolates QH0692, SS1196, SF162, 6101, BX08, BG1168, BAL were assayed with post-injection 5 serum; other HIV-1 isolates were assayed with post-injection 4 serum. ND = not done.

HIV+ sera was either HIV-1+ human serum (LEH3) or an anti-gp120 guinea pig serum (#) with known neutralizing activity for HIV-1 isolate SS1196. GMT = geometric mean titer of four animals per group. Neutralizing titers reported are after subtraction of any background neutralization in prebleed sera.

‡TriMab$_2$ = a mixture of human mabs 2F5, b12, 2G12.

CONCLUSIONS

The production of an artificial HIV-1 Group M consensus *env* genes (encoding sequences) (CON6 and Con-S) have been described that encodes a functional Env protein that is capable of utilizing the CCR5 co-receptor for mediating viral entry. Importantly, these Group M consensus envelope genes could induce T and B cell responses that recognized epitopes of subtype B and C HIV-1 primary isolates. In addition, Con-S induces antibodies that strongly neutralize Subtype-C and A HIV-1 strains (see Table 3).

The correlates of protection to HIV-1 are not conclusively known. Considerable data from animal models and studies in HIV-1-infected patients suggest the goal of HIV-1 vaccine development should be the induction of broadly-reactive CD4+ and CD8+ anti-HIV-1 T cell responses (Letvin et al, Annu. Rev. Immunol. 20:73-99 (2002)) and high levels of antibodies that neutralize HIV-1 primary isolates of multiple subtypes (Mascola et al, J. Virol. 73:4009-4018 (1999), Mascola et al, Nat. Med. 6:270-210 (2000)).

The high level of genetic variability of HIV-1 has made it difficult to design immunogens capable of inducing immune responses of sufficient breadth to be clinically useful. Epitope based vaccines for T and B cell responses (McMichael et al, Vaccine 20:1918-1921 (2002), Sbai et al, Curr. Drug Targets Infect, Disord. 1:303-313 (2001), Haynes, Lancet

348:933-937 (1996)), constrained envelopes reflective of fusion intermediates (Fouts et al, Proc. Natl. Acad. Sci. USA 99:11842-22847 (2002)), as well as exposure of conserved high-order structures for induction of anti-HIV-1 neutralizing antibodies have been proposed to overcome HIV-1 variability (Roben et al, J. Virol. 68:4821-4828 (1994), Saphire et al, Science 293:1155-1159 (2001)). However, with the ever-increasing diversity and rapid evolution of HIV-1, the virus is a rapidly moving complex target, and the extent of complexity of HIV-1 variation makes all of these approaches problematic. The current most common approach to HIV-1 immunogen design is to choose a wild-type field HIV-1 isolate that may or may not be from the region in which the vaccine is to be tested. Polyvalent envelope immunogens have been designed incorporating multiple envelope immunogens (Bartlett et al, AIDS 12:1291-1300 (1998), Cho et al, J. Virol. 75:2224-2234 (2001)).

The above-described study tests a new strategy for HIV-1 immunogen design by generating a group M consensus *env* gene (CON6) with decreased genetic distance between this candidate immunogen and wild-type field virus strains. The CON6 *env* gene was generated for all subtypes by choosing the most common amino acids at most positions (Gaschen et al, Science 296:2354-2360 (2002), Korber et al, Science 288:1789-1796 (2000)). Since only the most common amino acids were used, the majority of antibody and T cell epitopes were well preserved. Importantly,

the genetic distances between the group M consensus *env* sequence and any subtype *env* sequences was about 15%, which is only half of that between wild-type subtypes (30%) (Gaschen et al, Science 296:2354-2360 (2002)). This distance is approximately the same as that among viruses within the same subtype. Further, the group M consensus *env* gene was also about 15% divergent from any recombinant viral *env* gene, as well, since CRFs do not increase the overall genetic divergence among subtypes.

Infectivity of CON6-Env pseudovirions was confirmed using a single-round infection system, although the infectivity was compromised, indicating the artificial envelope was not in an "optimal" functional conformation, but yet was able to mediate virus entry. That the CON6 envelope used CCR5 (R5) as its coreceptor is important, since majority of HIV-1 infected patients are initially infected with R5 viruses.

BIAcore analysis showed that both CON6 gp120 and gp140CF bound sCD4 and a number of mabs that bind to wild-type HIV-1 Env proteins. The expression of the CON6 gp120 and 140CF proteins that are similar antigenically to wild-type HIV-1 envelopes is an important step in HIV-1 immunogen development. However, many wild-type envelope proteins express the epitopes to which potent neutralizing human mabs bind, yet when used as immunogens themselves, do not induce broadly neutralizing anti-HIV-1 antibodies of the specificity of the neutralizing human mabs.

The neutralizing antibody studies were encouraging in that both CON6 gp120, CON6 gp140CF and Con-S gp140CFI induced antibodies that neutralized select subtype B, C and D HIV-1 primary isolates, with Con-S gp140CFI inducing the most robust neutralization of non-subtype B primary HIV isolates. However, it is clear that the most difficult-to-neutralize primary isolates (PAVO, 6101, BG1168, 92RW020, CM244) were either only weakly or not neutralized by anti-CON6 gp120 or gp140 sera (Table 4b). Nonetheless, the Con-S envelope immunogenicity for induction of neutralizing antibodies is promising, given the breadth of responses generated with the Con-S subunit gp140CFI envelope protein for non-subtype B HIV isolates. Previous studies with poxvirus constructs expressing gp120 and gp160 have not generated high levels of neutralizing antibodies (Evans et al, J. Infect. Dis. 180:290-298 (1999), Polacino et al, J. Virol. 73:618-630 (1999), Ourmanov et al, J. Virol. 74:2960-2965 (2000), Pal et al, J. Virol 76:292-302 (2002), Excler and Plotkin, AIDS 11(Suppl A):S127-137 (1997). rVV expressing secreted CON6 gp120 and gp140 have been constructed and antibodies that neutralize HIV-1 primary isolates induced. An HIV neutralizing antibody immunogen can be a combination of Con-S gp140CFI, or subunit thereof, with immunogens that neutralize most subtype B isolates.

The structure of an oligomeric gp140 protein is critical when evaluating protein immunogenicity. In this regard, study of purified CON6 gp140CF proteins by fast performance liquid chromatography (FPLC) and analytical ultracentrifiguration has demonstrated that the purified gp140 peak consists predominantly of trimers with a small component of dimers.

Thus, centralized envelopes such as CON6, Con-S or 2003 group M or subtype consensus or ancestral encoding sequences described herein, are attractive candidates for preparation of various potentially "enhanced" envelope immunogens including CD4-Env complexes, constrained envelope structures, and trimeric oligomeric forms. The ability of CON6-induced T and B cell responses to protect against HIV-1 infection and/or disease in SHIV challenge models will be studied in non-human primates.

The above study has demonstrated that artificial centralized HIV-1 genes such as group M consensus *env* gene (CON6) and Con-S can also induce T cell responses to T cell epitopes in wild-type subtype B and C Env proteins as well as to those on group M consensus Env proteins (Figure 5). While the DNA prime and rVV boost regimen with CON6 gp140CF immunogen clearly induced IFN-γ producing T cells that recognized subtype B and C epitopes, further studies are needed to determine if centralized sequences such as are found in the CON6 envelope are significantly better at inducing cross-clade T cell responses than wild-type HIV-1 genes

(Ferrari et al, Proc. Natl. Acad. Sci. USA 94:1396-1401 (1997), Ferrari et al, AIDS Res. Hum. Retroviruses 16:1433-1443 (2000)). However, the fact that CON6 (and Con-S *env* encoding sequence) prime and boosted splenocyte T cells recognized HIV-1 subtype B and C T cell epitopes is an important step in demonstration that CON6 (and Con-S) can induce T cell responses that might be clinically useful.

Three computer models (consensus, ancestor and center of the tree (COT)) have been proposed to generate centralized HIV-1 genes (Gaschen et al, Science 296:2354-2360 (2002), Gao et al, Science 299:1517-1518 (2003), Nickle et al, Science 299:1515-1517 (2003), Korber et al, Science 288:1789-1796 (2000). They all tend to locate at the roots of the star-like phylogenetic trees for most HIV-1 sequences within or between subtypes. As experimental vaccines, they all can reduce the genetic distances between immunogens and field virus strains. However, consensus, ancestral and COT sequences each have advantages and disadvantages (Gaschen et al, Science 296:2354-2360 (2002), Gao et al, Science 299:1517-1518 (2003), Nickle et al, Science 299:1515-1517 (2003). Consensus and COT represent the sequences or epitopes in sampled current wild-type viruses and are less affected by outliers HIV-1 sequences, while ancestor represents ancestral sequences that can be significantly affected by outlier sequences. However, at present, it is not known which centralized sequence can serve

as the best immunogen to elicit broad immune responses against diverse HIV-1 strains, and studies are in progress to test these different strategies.

Taken together, the data have shown that the HIV-1 artificial CON6 and Con-S envelope can induce T cell responses to wild-type HIV-1 epitopes, and can induce antibodies that neutralize HIV-1 primary isolates, thus demonstrating the feasibility and promise of using artificial centralized HIV-1 sequences in HIV-1 vaccine design.

EXAMPLE 2

HIV-1 Subtype C Ancestral and Consensus Envelope Glycoproteins

EXPERIMENTAL DETAILS

HIV-1 subtype C ancestral and consensus *env* genes were obtained from the Los Alamos HIV Molecular Immunology Database (http://hiv-web.lanl.gov/immunology), codon-usage optimized for mammalian cell expression, and synthesized (Fig. 6). To ensure optimal expression, a Kozak sequence (GCCGCCGCC) was inserted immediately upstream of the initiation codon. In addition to the full-length genes, two truncated *env* genes were generated by introducing stop codons immediately after the gp41 membrane-spanning domain (IVNR) and the gp120/gp41 cleavage site (REKR), generating gp140 and gp120 form of the glycoproteins, respectively (Fig. 8).

Genes were tested for integrity in an *in vitro* transcription/translation system and expressed in mammalian cells. To determine if the ancestral and consensus subtype C envelopes were capable of mediating fusion and entry, *gp160* and *gp140* genes were co-transfected with an HIV-1/SG3Δ*env* provirus and the resulting pseudovirions tested for infectivity using the JC53-BL cell assay (Fig. 7). Co-receptor usage and envelope neutralization sensitivity were also determined with slight modifications of the JC53-BL assay. Codon-usage optimized and rev-dependent 96ZAM651 *env* genes were used as contemporary subtype C controls.

RESULTS

Codon-optimized subtype C ancestral and consensus envelope genes (*gp160, gp140, gp120*) express high levels of *env* glycoprotein in mammalian cells (Fig. 9).

Codon-optimized subtype C *gp160* and *gp140* glycoproteins are efficiently incorporated into virus particles. Western Blot analysis of sucrose-purified pseudovirions reveals ten-fold higher levels of virion incorporation of the codon-optimized envelopes compared to that of a rev-dependent contemporary envelope controls (Fig. 10A).

Virions pseudotyped with either the subtype C consensus *gp160* or *gp140* envelope were more infectious than pseudovirions containing the corresponding gp160 and gp140 ancestral envelopes.

Additionally, *gp160* envelopes were consistently more infectious than their respective *gp140* counterparts (Fig. 10B).

Both subtype C ancestral and consensus envelopes utilize CCR5 as a co-receptor to mediate virus entry (Fig. 11).

The infectivity of subtype C ancestral and consensus *gp160* containing pseudovirions was neutralized by plasma from subtype C infected patients. This suggests that these artificial envelopes possess a structure that is similar to that of native HIV-1 *env* glycoproteins and that common neutralization epitopes are conserved. No significant differences in neutralization potential were noted between subtype C ancestral and consensus *env* glycoproteins (gp160) (Fig. 12).

CONCLUSIONS

HIV-1 subtype C viruses are among the most prevalent circulating isolates, representing approximately fifty percent of new infections worldwide. Genetic diversity among globally circulating HIV-1 strains poses a challenge for vaccine design. Although HIV-1 Env protein is highly variable, it can induce both humoral and cellular immune responses in the infected host. By analyzing 70 HIV-1 complete subtype C *env* sequences, consensus and ancestral subtype C *env* genes have been generated. Both sequences are roughly equidistant from contemporary subtype C strains and thus

expected to induce better cross-protective immunity. A reconstructed ancestral or consensus sequence derived-immunogen minimizes the extent of genetic differences between the vaccine candidate and contemporary isolates. However, consensus and ancestral subtype C *env* genes differ by 5% amino acid sequences. Both consensus and ancestral sequences have been synthesized for analyses. Codon-optimized subtype C ancestral and consensus envelope genes have been constructed and the *in vitro* biological properties of the expressed glycoproteins determined. Synthetic subtype C consensus and ancestral *env* genes express glycoproteins that are similar in their structure, function and antigenicity to contemporary subtype C wild-type envelope glycoproteins.

EXAMPLE 3

Codon-Usage Optimization of Consensus of Subtype C *gag* and *nef* Genes (C.con.gag and C.con.nef)

Subtype C viruses have become the most prevalent viruses among all subtypes of Group M viruses in the world. More than 50% of HIV-1 infected people are currently carrying HIV-1 subtype C viruses. In addition, there is considerable intra-subtype C variability: different subtype C viruses can differ by as much as 10%, 6%, 17% and

16% of their Gag, Pol, Env and Nef proteins, respectively. Most importantly, the subtype C viruses from one country can vary as much as the viruses isolated from other parts of the world. The only exceptions are HIV-1 strains from India/China, Brazil and Ethiopia/Djibouti where subtype C appears to have been introduced more recently. Due to the high genetic variability of subtype C viruses even within a single country, an immunogen based on a single virus isolate may not elicit protective immunity against other isolates circulating in the same area.

Thus *gag* and *nef* gene sequences of subtype C viruses were gathered to generate consensus sequences for both genes by using a 50% consensus threshold. To avoid a potential bias toward founder viruses, only one sequence was used from India/China, Brazil and Ethiopia/Djibouti, respectively, to generate the subtype C consensus sequences (C.con.gag and C.con.nef). The codons of both C.con.gag and C.con.nef genes were optimized based on the codon usage of highly expressed human genes. The protein expression following transfection into 293T cells is shown in Figure 13. As can be seen, both consensus subtype C Gag and Nef proteins were expressed efficiently and recognized by Gag- and Nef-specific antibodies. The protein expression levels of both C.con.gag and C.con.nef genes are comparible to that of native subtype *env* gene (96ZM651).

EXAMPLE 4

Synthesis of a Full Length "*Consensus of the Consensus env* Gene with Consensus Variable Regions" (CON-S)

In the synthesized "consensus of the consensus" *env* gene (CON6), the variable regions were replaced with the corresponding regions from a contemporary subtype C virus (98CN006). A further con/con gene has been designed that also has consensus variable regions (CON-s). The codons of the Con-S *env* gene were optimized based on the codon usage of highly expressed human genes. (See Figs. 14A and 14B for amino acid sequences and nucleic acid sequences, respectfully.)

Paired oligonucleotides (80-mers) which overlap by 20 bp at their 3' ends and contain invariant sequences at their 5' and 3' ends, including the restriction enzyme sites EcoRI and BbsI as well as BsmBI and BamHI, respectively, were designed. BbsI and BamHI are Type II restriction enzymes that cleave outside of their recognition sequences. They have been positioned in the oligomers in such a way that they cleave the first four resides adjacent to the 18 bp invariant region, leaving 4 base 5' overhangs at the end of each fragment for the following ligation step. 26 paired oligomers were linked individually using PCR and primers complimentary to the 18 bp invariant sequences.

Each pair was cloned into pGEM-T (Promega) using the T/A cloning method and sequenced to confirm the absence of inadvertent mutations/deletions. pGEM-T subclones containing the proper inserts were then digested, run on a 1% agarose gel, and gel purified (Qiagen). Four individual 108-mers were ligated into pcDNA3.1 (Invitrogen) in a multi-fragment ligation reaction. The four-way ligations occurred among groups of fragments in a stepwise manner from the 5' to the 3' end of the gene. This process was repeated until the entire gene was reconstructed in the pcDNA3.1 vector.

A complete Con-S gene was constructed by ligating the codon usage optimized oligo pairs together. To confirm its open reading frame, an *in vitro* transcription and translation assay was performed. Protein products were labeled by S^{35}-methionine during the translation step, separated on a 10% SDS-PAGE, and detected by radioautography. Expected size of the expressed Con-S gp160 was identified in 4 out of 7 clones (Fig. 14C).

CONs Env protein expression in the mammalian cells after transfected into 293T cells using a Western blot assay (Figure 15). The expression level of Con-S Env protein is very similar to what was observed from the previous CON6 *env* clone that contains the consensus conservative regions and variable loops from 98CN006 virus isolate.

The Env-pseudovirons was produced by cotransfecting Con-S *env* clone and *env*-deficient SG3

proviral clone into 293T cells. Two days after transfection, the pseudovirions were harvested and infected into JC53BL-13 cells. The infectious units (IU) were determined by counting the blue cells after staining with X-gal in three independent experiments. When compared with CON6 *env* clone, Con-S *env* clones produce similar number of IU in JC53BL-13 cells (Figure 16). The IU titers for both are about 3 log higher than the SG3 backbone clone control (No Env). However, the titers are also about 2 log lower than the positive control (the native HIV-1 *env* gene, NL4-3 or YU2). These data suggest that both *consensus* group M *env* clones are biologically functional. Their functionality, however, has been compromised. The functional consensus *env* genes indicate that these Env proteins fold correctly, preserve the basic conformation of the native Env proteins, and are able to be developed as universal Env immunogens.

It was next determined what coreceptor Con-S Env uses for its entry into JC53-BL cells. When treated with CXCR4 blocking agent AMD3100, the infectivity of NL4-3 Env-pseudovirons was blocked while the infectivity of YU2, Con-S or CON6 Env-pseudovirons was not inhibited. In contrast, when treated with CCR5 blocking agent TAK779, the infectivity of NL4-3 Env-pseudovirons was not affected, while the infectivity of YU2, Con-S or CON6 Env-pseudovirons was inhibited. When treated with both blocking agents, the infectivity of all pseudovirions was inhibited. Taken together, these

data show that the Con-S as well as CON6 envelope uses the CCR5 but not CXCR4 co-receptor for its entry into target cells.

It was next determined whether CON6 or Con-S Env proteins could be equally efficiently incorporated in to the pseudovirions. To be able precisely compare how much Env proteins were incorporated into the pseudovirions, each pseudovirions is loaded on SDS-PAGE at the same concentraion: 5µg total protein for cell lysate, 25ng p24 for cell culture supernatant, or 150ng p24 for purified virus stock (concentrated pseudovirions after super-speed centrifugation). There was no difference in amounts of Env proteins incorporated in CON6 or Con-S Env-pseudovirions in any preparations (cell lysate, cell culture supernatant or purified virus stock) (Figure 17).

EXAMPLE 5

Synthesis of a *Consensus* Subtype A Full Length *env* (A.con.env) Gene

Subtype A viruses are the second most prevalent HIV-1 in the African continent where over 70% of HIV-1 infections have been documented. Consensus *gag*, *env* and *nef* genes for subtype C viruses that are the most prevalent viruses in Africa and in the world were previously generated. Since genetic distances between subtype A and C viruses are as high as 30% in the *env* gene, the cross reactivity or protection between both subtypes will not be

optimal. Two group M consensus *env* genes for all subtypes were also generated. However, to target any particular subtype viruses, the subtype specific consensus genes will be more effective since the genetic distances between subtype consensus genes and field viruses from the same subtype will be smaller than that between group M consensus genes and these same viruses. Therefore, consensus genes need to be generated for development of subtype A specific immunogens. The codons of the A.con.env gene were optimized based on the codon usage of highly expressed human genes. (See Figs. 18A and 18B for amino acid and nucleic acid sequences, respectively.)

Each pair of the oligos has been amplified, cloned, ligated and sequenced. After the open reading frame of the A.con *env* gene was confirmed by an *in vitro* transcription and translation system, the A.con *env* gene was transfected into the 293T cells and the protein expression and specificity confirmed with the Western blot assay (Figure 18). It was then determined whether A.con envelope is biologically functional. It was co-transfected with the *env*-defective SG3 proviral clone into 293T cells. The pseudotyped viruses were harvested and used to infect JC53BL cells. Blue cells were detected in JC53-BL cells infected with the A.con Env-pseudovirions, suggesting that A.con Env protein is biologically functional (Table 6). However, the infectious titer of A.con Env-psuedovirions was about 7-fold lower than that of pseudovirions with

wild-type subtype C envelope (Table 6). Taken together, the biological function A.con Env proteins suggests that it folds correctly and may induce linear and conformational T and B cell epitopes if used as an Env immunogen.

JC53BL13 (IU/ul)

	3/31/03	4/7/03	4/25/03
	non filtered supt.	0.22µm filtered	0.22µm filtered
A.con +SG3	4	8.5	15.3
96ZM651 +SG3	87	133	104
SG3 backbone	0	0.07	0.03
Neg control	0	0.007	0

Table 6. Infectivity of pseudovirons with A.con env genes

EXAMPLE 6

Design of Full Length "*Consensus of the Consensus gag, pol and nef* Genes" (M.con.gag, M.con.pol and M.con.nef) and a Subtype C *Consensus* pol Gene (C.con.pol)

For the group M consensus genes, two different *env* genes were constructed, one with virus specific variable regions (CON6) and one with consensus variable regions (Con-S). However, analysis of T cell immune responses in immunized or vaccinated animals and humans shows that the *env* gene normally is not a main target for T cell immune response

although it is the only gene that will induce neutralizing antibody. Instead, HIV-1 Gag, Pol and Nef proteins are found to be important for inducing potent T cell immune responses. To generate a repertoire of immunogens that can induce both broader humoral and cellular immune responses for all subtypes, it may be necessary to construct other group M consensus genes other than *env* gene alone. "*Consensus of the consensus*" *gag*, *pol* and *nef* genes (M.con.gag., M.con.pol and M.con.nef) have been designed. To generate a subtype consensus pol gene, the subtype C consensus *pol* gene (C.con.pol) was also designed. The codons of the M.con.gag., M.con.pol, M.con.nef and C.con.pol. genes were optimized based on the codon usage of highly expressed human genes. (See Fig. 19 for nucleic acid and amino acid sequences.)

EXAMPLE 7

Synthetic Subtype B Consensus *gag* and *env* Genes

EXPERIMENTAL DETAILS

Subtype B consensus *gag* and *env* sequences were derived from 37 and 137 contemporary HIV-1 strains, respectively, codon-usage optimized for mammalian cell expression, and synthesized (Figs. 20A and 20B). To ensure optimal expression, a Kozak sequence (GCCGCCGCC) was inserted immediately upstream of the initiation codon. In addition to the full-length *env* gene, a truncated *env* gene was generated by introducing a stop codon immediately

after the gp41 membrane-spanning domain (IVNR) to create a *gp145* gene. Genes were tested for integrity in an *in vitro* transcription/translation system and expressed in mammalian cells. (Subtype B consensus Gag and Env sequences are set forth in Figs. 20C and 20D, respectively.)

To determine if the subtype B consensus envelopes were capable of mediating fusion and entry, *gp160* and *gp145* genes were co-transfected with an HIV-1/SG3Δenv provirus and the resulting pseudovirions were tested for infectivity using the JC53-BL cell assay. JC53-BL cells are a derivative of HeLa cells that express high levels of CD4 and the HIV-1 coreceptors CCR5 and CXCR4. They also contain the reporter cassettes of luciferase and β-galactosidase that are each expressed from an HIV-1 LTR. Expression of the reporter genes is dependent on production of HIV-1 Tat. Briefly, cells are seeded into 24-well plates, incubated at 37°C for 24 hours and treated with DEAE-Dextran at 37°C for 30min. Virus is serially diluted in 1% DMEM, added to the cells incubating in DEAE-dextran, and allowed to incubate for 3 hours at 37°C after which an additional 500μL of cell media is added to each well. Following a final 48-hour incubation at 37°C, cells are fixed, stained using X-Gal, and overlaid with PBS for microscopic counting of blue foci. Counts for mock-infected wells, used to determine background, are subtracted from counts for the sample wells. Co-receptor usage and envelope

neutralization sensitivity were also determined with slight modifications of the JC53-BL assay.

To determine whether the subtype B consensus Gag protein was capable of producing virus-like particles (VLPs) that incorporated Env glycoproteins, 293T cells were co-transfected with subtype B consensus *gag* and *env* genes. 48-hours post-transfection, cell supernatants containing VLPs were collected, clarified in a tabletop centrifuge, filtered through a 0.2mM filter, and pellet through a 20% sucrose cushion. The VLP pellet was resuspended in PBS and transferred onto a 20-60% continuous sucrose gradient. Following overnight centrifugation at 100,000 x g, 0.5 ml fractions were collected and assayed for p24 content. The refractive index of each fraction was also measured. Fractions with the correct density for VLPs and containing the highest levels of p24 were pooled and pellet a final time. VLP-containing pellets were re-suspended in PBS and loaded on a 4-20% SDS-PAGE gel. Proteins were transferred to a PVDF membrane and probed with serum from a subtype B HIV-1 infected individual.

RESULTS

Codon-usage optimized, subtype B consensus envelope (*gp160, gp145*) and *gag* genes express high levels of glycoprotein in mammalian cells (Fig. 21).

Subtype B gp160 and gp145 glycoproteins are efficiently incorporated into virus particles.

Western Blot analysis of sucrose-purified pseudovirions suggests at least five-fold higher levels of consensus B envelope incorporation compared to incorporation of a rev-dependent contemporary envelope (Fig.23A). Virions pseudotyped with either the subtype B consensus gp160 or gp145 envelope are more infectious than pseudovirions containing a rev-dependent contemporary envelope (Fig. 23 B).

Subtype B consensus envelopes utilize CCR5 as the co-receptor to gain entry into CD4 bearing target cells (Fig. 22).

The infectivity of pseudovirions containing the subtype B consensus gp160 envelope was neutralized by plasma from HIV-1 subtype B infected patients (Fig. 24C) and neutralizing monoclonal antibodies (Fig. 24A). This suggests that the subtype B synthetic consensus B envelopes is similar to native HIV-1 Env glycoproteins in its overall structure and that common neutralization epitopes remain intact. Figs. 24B and 24D show neutralization profiles of a subtype B control envelope (NL4.3 Env).

Subtype B consensus Gag proteins are able to bud from the cell membrane and form virus-like particles (Fig. 25A). Co-transfection of the codon-optimized subtype B consensus *gag* and *gp160* genes produces VLPs with incorporated envelope (Fig. 25B).

CONCLUSIONS

The synthetic subtype B consensus *env* and *gag* genes express viral proteins that are similar in their structure, function and antigenicity to contemporary subtype B Env and Gag proteins. It is contemplated that immunogens based on subtype B consensus genes will elicit CTL and neutralizing immune responses that are protective against a broad set of HIV-1 isolates.

* * *

All documents and other information sources cited above are hereby incorporated in their entirety by reference.

ABSTRACT

The present invention relates, in general, to an immunogen and, in particular, to an immunogen for inducing antibodies that neutralize a wide spectrum of HIV primary isolates and/or to an immunogen that induces a T cell immune response. The invention also relates to a method of inducing anti-HIV antibodies, and/or to a method of inducing a T cell immune response, using such an immunogen. The invention further relates to nucleic acid sequences encoding the present immunogens.

A

MRVMGIQRNCQHLWRWGTMILGMLMICSAAENLWVTVYYGVPVWKEANTTLFCASDAKAYDTEVHNVWAT

V1

HACVPTDPNPQEIVLENVTENFNMWKNNMVEQMHEDIISLWDQSLKPCVKLTPLCVTLNCTNVRNVSSNG

V2

TETDNEEIKNCSFNITTELRDKKQKVYALFYRLDVVPIDDKNSSEISGKNSSEYYRLINCNTSAITQACP

KVSFEPIPIHYCAPAGFAILKCNDKKFNGTGPCKNVSTVQCTHGIKPVVSTQLLLNGSLAEEEIIIRSEN

V3

ITNNAKTIIVQLNESVEINCTRPNNNTRKSIHIGPGQAFYATGEIIGDIRQAHCNISRTKWNKTLQQVAK

V4

KLREHFNNKTIIFKPSSGGDLEITTHSFNCGGEFFYCNTSGLFNSTWMFNGTYMFNGTKDNSETITLPCR

V5

IKQIINMWQGVGQAMYAPPIEGKITCKSNITGLLLTRDGGNNSNKNKTETFRPGGGDMRDNWRSELYKYK

VVKIEPLGVAPTKAKRRVVEREKRAVGIGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLR

AIEAQQHLLQLTVWGIKQLQARVLAVERYLKDQQLLGIWGCSGKLICTTNVPWNSSWSNKSQDEIWDNMT

WMEWEREISNYTDIIYRLIEESQNQQEKNEQELLALDKWASLWNWFDITNWLWYIKIFIMIVGGLIGLRI

VFAVLSIVNRVRQGYSPLSFQTLIPNPRGPDRPEGIEEEGGEQGRDRSIRLVNGFLALAWDDLRSLCLFS

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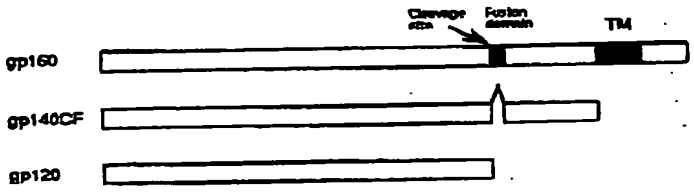
B



C

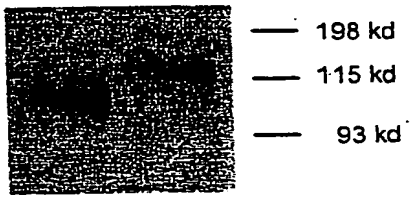


Figure 1

CON6.env (group M env consensus. This one contain five variable regions in env gene from 98CN006 virus, not in the public domain yet)

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CTGGGCATGCTGATGATCTGCTCCGCCGCCGAGAACCTGTGGGTGACCGTGTACTACGGC
GTGCCCGTGTGGAAGGAGGCCAACACCACCCTGTTCTGCGCCTCCGACGCCAAGGCCTAC
GACACCGAGGTGCACAACGTGTGGGCCACCCACGCCTGCGTGCCCACCGACCCCAACCCC
CAGGAGATCGTGCTGGAGAACGTGACCGAGAACTTCAACATGTGGAAGAACAACATGGTG
GAGCAGATGCACGAGGACATCATCTCCCTGTGGGACCAGTCCCTGAAGCCCTGCGTGAAG
CTGACCCCCCTGTGCGTGACCCTGAACTGCACCAACGTGCGCAACGTGTCCTCCAACGGC
ACCGAGACCGACAACGAGGAGATCAAGAACTGCTCCTTCAACATCACCACCGAGCTGCGC
GACAAGAAGCAGAAGGTGTACGCCCTGTTCTACCGCCTGGACGTGGTGCCCATCGACGAC
AAGAACTCCTCCGAGATCTCCGGCAAGAACTCCTCCGAGTACTACCGCCTGATCAACTGC
AACACCTCCGCCATCACCCAGGCCTGCCCCAAGGTGTCCTTCGAGCCCATCCCCATCCAC
TACTGCGCCCCCGCCGGCTTCGCCATCCTGAAGTGCAACGACAAGAAGTTCAACGGCACC
GGCCCCTGCAAGAACGTGTCCACCGTGCAGTGCACCCACGGCATCAAGCCCGTGGTGTCC
ACCCAGCTGCTGCTGAACGGCTCCCTGGCCGAGGAGGAGATCATCATCCGCTCCGAGAAC
ATCACCAACAACGCCAAGACCATCATCGTGCAGCTGAACGAGTCCGTGGAGATCAACTGC
ACCCGCCCCAACAACAACACCCGCAAGTCCATCCACATCGGCCCCGGCCAGGCCTTCTAC
GCCACCGGCGAGATCATCGGCGACATCCGCCAGGCCCACTGCAACATCTCCCGCACCAAG
TGGAACAAGACCCTGCAGCAGGTGGCCAAGAAGCTGCGCGAGCACTTCAACAACAAGACC
ATCATCTTCAAGCCCTCCTCCGGCGGCGACCTGGAGATCACCACCCACTCCTTCAACTGC
GGCGGCGAGTTCTTCTACTGCAACACCTCCGGCCTGTTCAACTCCACCTGGATGTTCAAC
GGCACCTACATGTTCAACGGCACCAAGGACAACTCCGAGACCATCACCCTGCCCTGCCGC
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AACAACTCCAACAAGAACAAGACCGAGACCTTCCGCCCCGGCGGCGGCGACATGCGCGAC
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GTGTTCCTGGGCTTCCTGGGCGCCGCCGGCTCCACCATGGGCGCCGCCTCCATCACCCTG
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GCCCGCGTGCTGGCCGTGGAGCGCTACCTGAAGGACCAGCAGCTGCTGGGCATCTGGGGC
TGCTCCGGCAAGCTGATCTGCACCACCAACGTGCCCTGGAACTCCTCCTGGTCCAACAAG
TCCCAGGACGAGATCTGGGACAACATGACCTGGATGGAGTGGGAGCGCGAGATCTCCAAC
TACACCGACATCATCTACCGCCTGATCGAGGAGTCCCAGAACCAGCAGGAGAAGAACGAG
CAGGAGCTGCTGGCCCTGGACAAGTGGGCCTCCCTGTGGAACTGGTTCGACATCACCAAC
TGGCTGTGGTACATCAAGATCTTCATCATGATCGTGGGCGGCCTGATCGGCCTGCGCATC
GTGTTCGCCGTGCTGTCCATCGTGAACCGCGTGCGCCAGGGCTACTCCCCCCCTGTCCTTC
CAGACCCTGATCCCCAACCCCCGCGGCCCCGACCGCCCCGAGGGCATCGAGGAGGAGGGC
GGCGAGCAGGGCCGCGACCGCTCCATCCGCCTGGTGAACGGCTTCCTGGCCCTGGCCTGG
GACGACCTGCGCTCCCTGTGCCTGTTCTCCTACCACCGCCTGCGCGACTTCATCCTGATC
GCCGCCCGCACCGTGGAGCTGCTGGGCCGCCGCTCCCTGCGCGGCCTGCAGAAGGGCTGG
GAGGCCCTGAAGTACCTGGGCAACCTGCTGCAGTACTGGGGCCAGGAGCTGAAGAACTCC
GCCATCTCCCTGCTGGACACCACCGCCATCGCCGTGGCCGAGGGCACCGACCGCGTGATC
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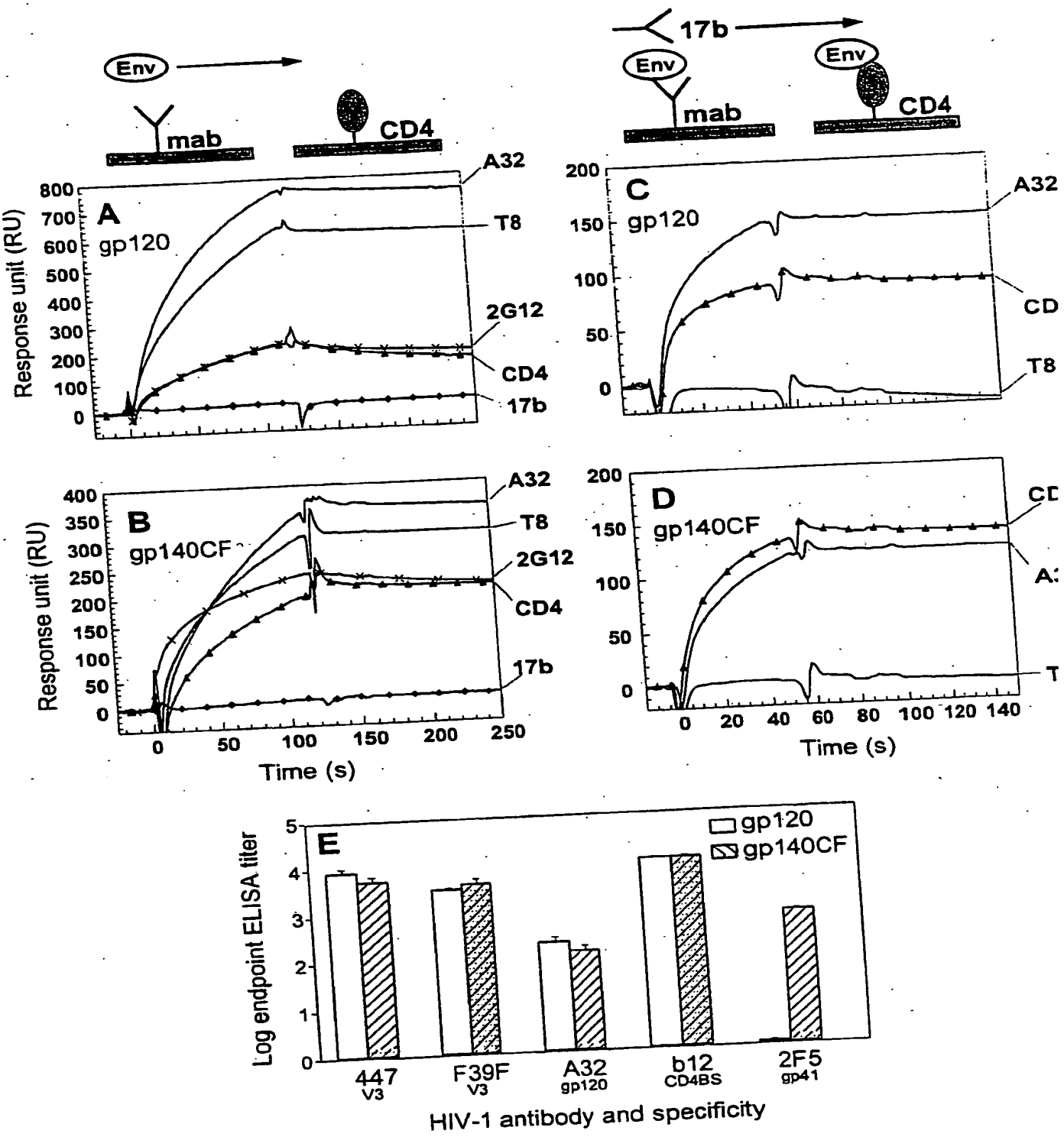
CTGGAGCGCGCCCTGCTGTAA

Figure 1D


Env
mab
CD4
17b
A
gp120
B
gp140CF
C
gp120
D
gp140CF
A32
T8
2G12
CD4
17b
Response unit (RU)
Time (s)
E
gp120
gp140CF
Log endpoint ELISA titer
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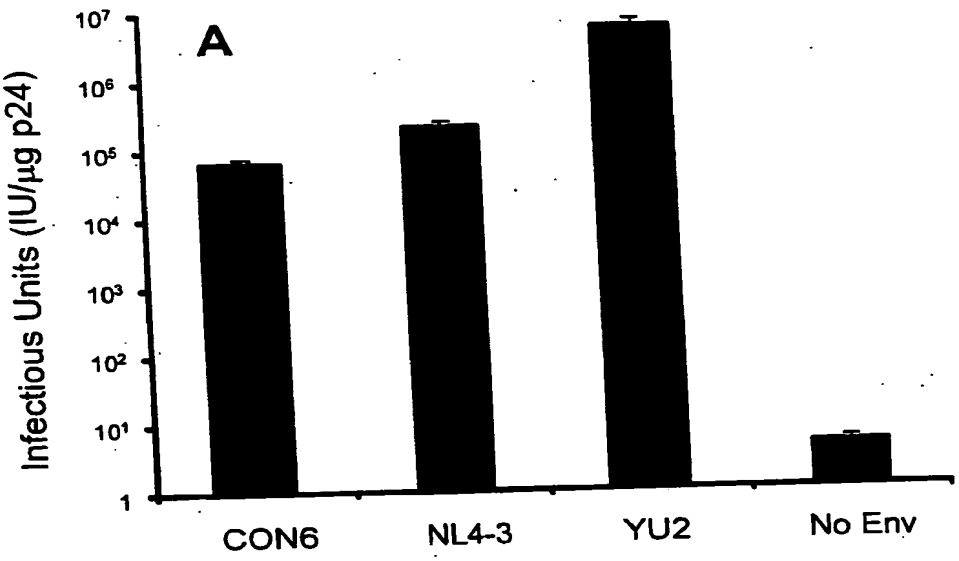
V3
F39F
V3
A32
gp120
b12
CD4BS
2F5
gp41
HIV-1 antibody and specificity

Figure 2


A
Infectious Units (IU/µg p24)
10⁷
10⁶
10⁵
10⁴
10³
10²
10¹
1
CON6
NL4-3
YU2
No Env

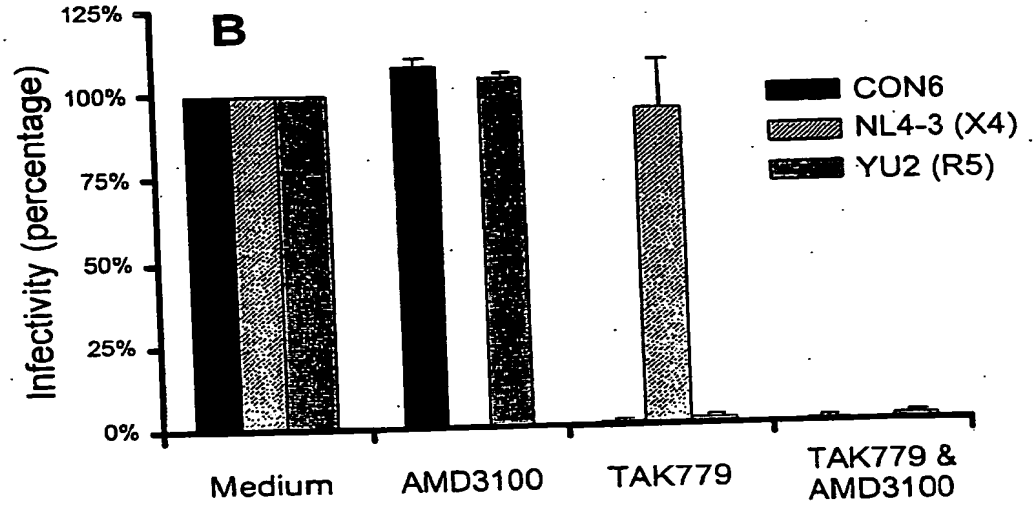
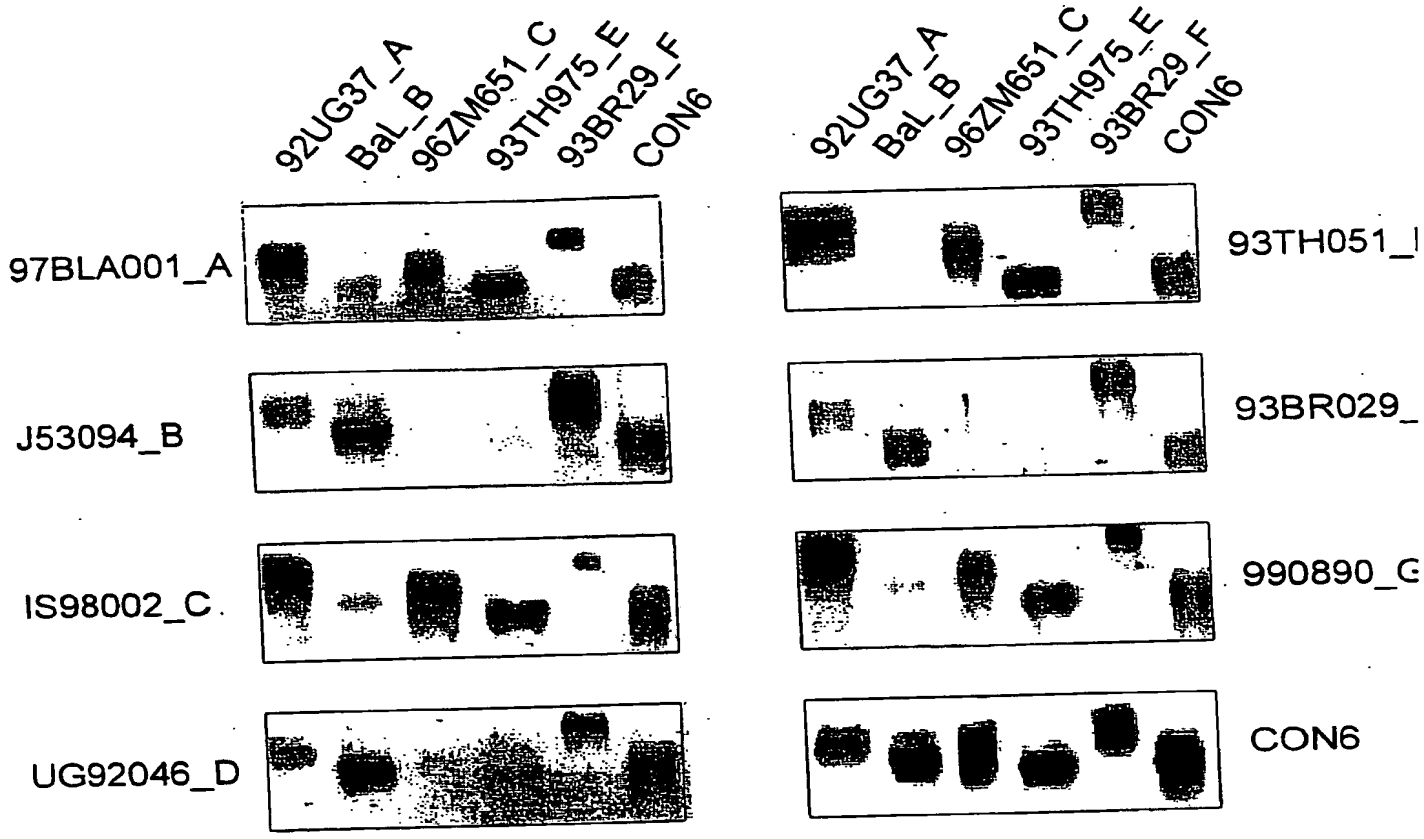

B
Infectivity (percentage)
125%
100%
75%
50%
25%
0%
CON6
NL4-3 (X4)
YU2 (R5)
Medium
AMD3100
TAK779
TAK779 &
AMD3100

Figure 3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93BR29_F
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CON6

Figure 4

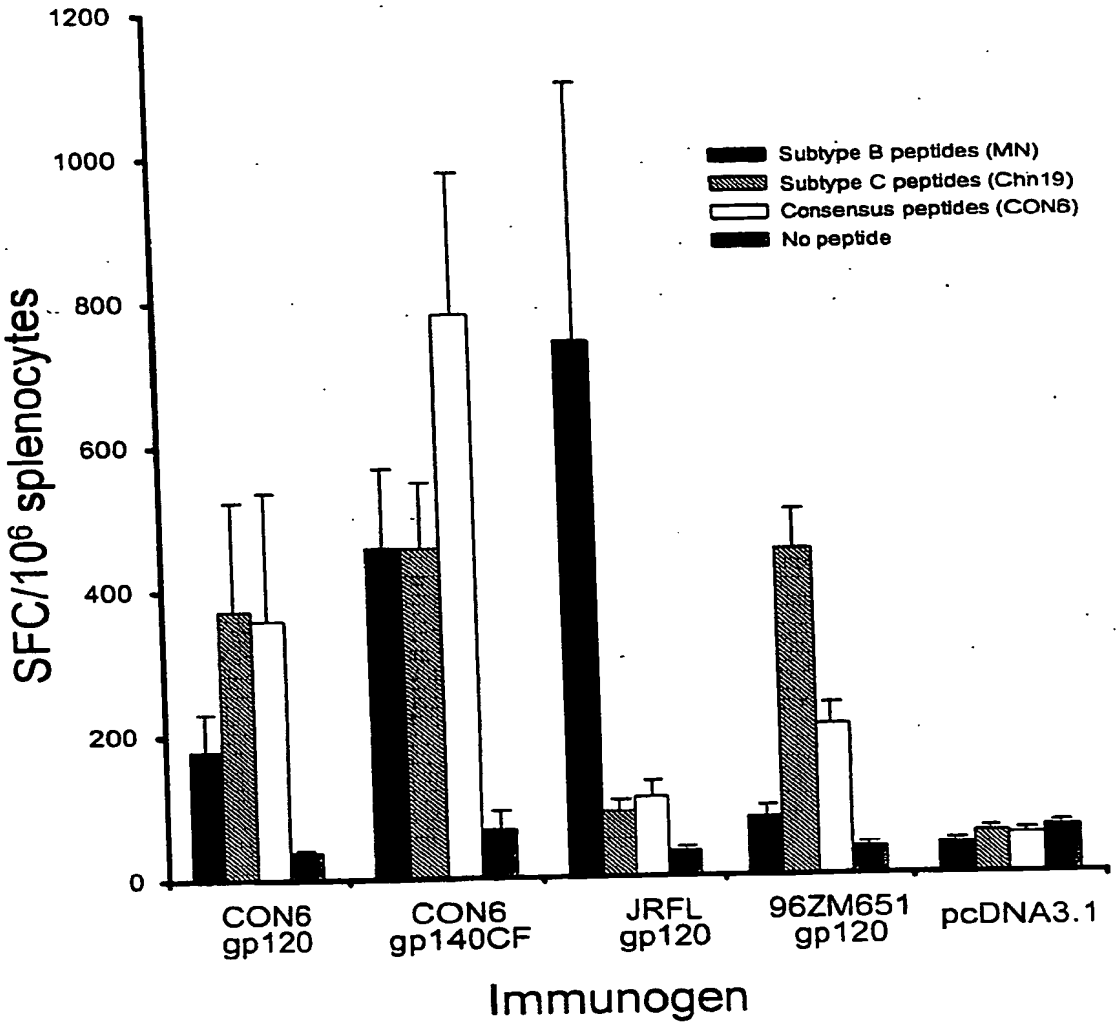
1200
1000
800
600
400
200
0
SFC/10^6 splenocytes
Subtype B peptides (MN)
Subtype C peptides (Chn19)
Consensus peptides (CON6)
No peptide
CON6 gp120
CON6 gp140CF
JRFL gp120
96ZM651 gp120
pcDNA3.1
Immunogen

Figure 5

Figure 6A

C.anc.env (subtype C ancestral env. The amino acid sequence is different from Los Alamos Database August 2002)

GCCGCCATGCGCGTGATGGGCATCCTGCGCAACTGCCAGCAGTGGTGGAT
CTGGGGCATCCTGGGCTTCTGGATGCTGATGATCTGCTCCGTGGTGGGCA
ACCTGTGGGTGACCGTGTACTACGGCGTGCCCGTGTGGAAGGAGGCCAAG
ACCACCCTGTTCTGCGCCTCCGACGCCAAGGCCTACGAGCGCGAGGTGCA
CAACGTGTGGGCCACCCACGCCTGCGTGCCCACCGACCCCAACCCCCAGG
AGATGGTGCTGGAGAACGTGACCGAGAACTTCAACATGTGGAAGAACGAC
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GTGTCCTTCGACCCCATCCCCATCCACTACTGCGCCCCCGCCGGCTACGC
CATCCTGAAGTGCAACAACAAGACCTTCAACGGCACCGGCCCCTGCAACA
ACGTGTCCACCGTGCAGTGCACCCACGGCATCAAGCCCGTGGTGTCCACC
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CGAGAACCTGACCGACAACGCCAAGACCATCATCGTGCAGCTGAACGAGT
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CATCCGCCAGGCCCACTGCAACATCTCCGAGGACAAGTGGAACAAGACCC
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CGCATCAAGCAGATCATCAACATGTGGCAGGGCGTGGGCCAGGCCATGTA
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TGCTGCTGACCCGCGACGGCGGCAAGGAGAACACCACCGAGACCTTCCGC
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CAAGGTGGTGGAGATCAAGCCCCTGGGCGTGGCCCCCACCGAGGCCAAGC
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GACGACATCTGGGACAACATGACCTGGATGGAGTGGGACCGCGAGATCTC
CAACTACACCGACACCATCTACCGCCTGCTGGAGGAGTCCCAGAACCAGC
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CCGCTCCTCCCTGCGCGGCCTGCAGCGCGGCTGGGAGGCCCTGAAGTACC
TGGGCTCCCTGGTGCAGTACTGGGGCCAGGAGCTGAAGAAGTCCGCCATC
TCCCTGCTGGACACCATCGCCATCGCCGTGGCCGAGGGCACCGACCGCAT
CATCGAGGTGGTGCAGCGCGCCTGCCGCGCCATCCTGAACATCCCCCGCC
GCATCCGCCAGGGCTTCGAGGCCGCCCTGCTGTAA

Figure 6B

C.con.env (subtype C consensus env. The amino acid sequence is different from Los Alamos Database August 2002)

GCCGCCATGCGCGTGATGGGCATCCTGCGCAACTGCCAGCAGTGGTGGAT
CTGGGGCATCCTGGGCTTCTGGATGCTGATGATCTGCAACGTGGTGGGCA
ACCTGTGGGTGACCGTGTACTACGGCGTGCCCGTGTGGAAGGAGGCCAAG
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TGCTGCTGACCCGCGACGGCGGCAAGAAGAACACCACCGAGATCTTCCGC
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GCCGCGTGGTGGAGCGCGAGAAGCGCGCCGTGGGCATCGGCGCCGTGTTC
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GAGGACATCTGGGACAACATGACCTGGATGCAGTGGGACCGCGAGATCTC
CAACTACACCGACACCATCTACCGCCTGCTGGAGGACTCCCAGAACCAGC
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CATGATCGTGGGCGGCCTGATCGGCCTGCGCATCATCTTCGCCGTGCTGT
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CGCCTGCGCGACTTCATCCTGGTGGCCGCCCGCGCCGTGGAGCTGCTGGG
CCGCTCCTCCCTGCGCGGCCTGCAGCGCGGCTGGGAGGCCCTGAAGTACC
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TCCCTGCTGGACACCATCGCCATCGCCGTGGCCGAGGGCACCGACCGCAT
CATCGAGCTGATCCAGCGCATCTGCCGCGCCATCCGCAACATCCCCCGCC
GCATCCGCCAGGGCTTCGAGGCCGCCCTGCAGTAA

Figure 6C

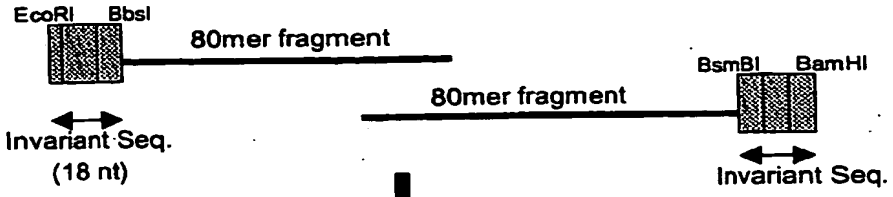
C.anc.env (subtype C ancestral env)
MRVMGILRNCQQWWIWGILGFWMLMICSVVGNLWVTVYYGVPVWKEAKTTLFCASDAKAYEREVHNVWAT
HACVPTDPNPQEMVLENVTENFNMWKNDMVDQMHEDIISLWDQSLKPCVKLTPLCVTLNCTNVTNATNNT
YNGEMKNCSFNITTELRDKKKKEYALFYRLDIVPLNENSSEYRLINCNTSAITQACPKVSFDPIPIHYCA
PAGYAILKCNNKTFNGTGPCNNVSTVQCTHGIKPVVSTQLLLNGSLAEEEIIIRSENLTDNAKTIIVQLN
ESVEIVCTRPNNNTRKSMRIGPGQTFYATGDIIGDIRQAHCNISEDKWNKTLQQVAEKLGKHFPNKTITF
EPSSGGDLEITTHSFNCRGEFFYCNTSKLFNSTYNNNTNSNSTITLPCRIKQIINMWQGVGQAMYAPPIA
GNITCKSNITGLLLTRDGGKENTTETFRPGGGDMRDNWRSELYKYKVVEIKPLGVAPTEAKRRVVEREKR
AVGLGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLRAIEAQQHMLQLTVWGIKQLQARVL
AMERYLKDQQLLGIWGCSGKLICTTAVPWNSSWSNKSLDDIWDNMTWMEWDREISNYTDTIYRLLEESQN
QQEKNEQDLLALDSWENLWNWFDITNWLWYIKIFIMIVGGLIGLRIIFAVLSIVNRVRQGYSPLSFQTLT
PNPRGPDRLERIEEEGGEQDRDRSIRLVSGFLALAWDDLRSLCLFSYHRLRDFILIAARTVELLGRSSLR
GLQRGWEALKYLGSLVQYWGQELKKSAISLLDTIAIAVAEGTDRIIEVVQRACRAILNIPRRIRQGFEAA
LL

Figure 6D

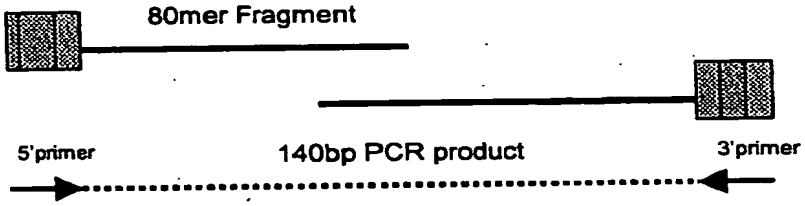
C.con.env (subtype C consensus env)
MRVMGILRNCQQWWIWGILGFWMLMICNVVGNLWVTVYYGVPVWKEAKTTLFCASDAKAYEKEVHNVWAT
HACVPTDPNPQEMVLENVTENFNMWKNDMVDQMHEDIISLWDQSLKPCVKLTPLCVTLNCRNVTNATNNT
YNEEIKNCSFNITTELRDKKKKVYALFYRLDIVPLNENSSEYRLINCNTSAITQACPKVSFDPIPIHYCA
PAGYAILKCNNKTFNGTGPCNNVSTVQCTHGIKPVVSTQLLLNGSLAEEEIIIRSENLTNNAKTIIVHLN
ESVEIVCTRPNNNTRKSIRIGPGQTFYATGDIIGDIRQAHCNISEDKWNKTLQRVSKKLKEHFPNKTIKF
EPSSGGDLEITTHSFNCRGEFFYCNTSKLFNSTYNNNTNSNSTITLPCRIKQIINMWQEVGRAMYAPPIA
GNITCKSNITGLLLTRDGGKKNTTEIFRPGGGDMRDNWRSELYKYKVVEIKPLGVAPTKAKRRVVEREKR
AVGIGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLRAIEAQQHMLQLTVWGIKQLQTRVL
AIERYLKDQQLLGIWGCSGKLICTTAVPWNSSWSNKSQEDIWDNMTWMQWDREISNYTDTIYRLLEDSQN
QQEKNEKDLLALDSWKNLWNWFDITNWLWYIKIFIMIVGGLIGLRIIFAVLSIVNRVRQGYSPLSFQTLT
PNPRGPDRLGRIEEEGGEQDRDRSIRLVSGFLALAWDDLRSLCLFSYHRLRDFILVAARAVELLGRSSLR
GLQRGWEALKYLGSLVQYWGLELKKSAISLLDTIAIAVAEGTDRIIELIQRICRAIRNIPRRIRQGFEAA
LQ

Figure 6E

Synthesize entire gene in 80-mer fragments overlapping by 20 residues at the 3' end with invariant sequences at the 5' end.

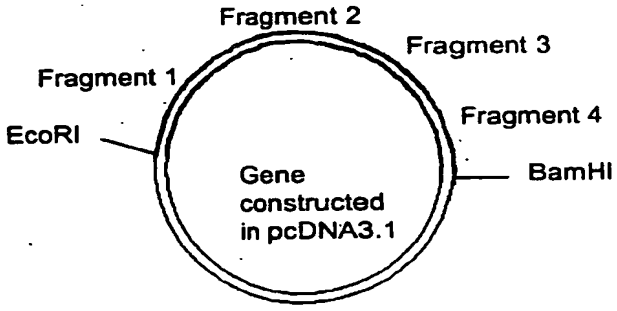


Paired 80mer oligos are connected via PCR in a stepwise manner from 5' to 3' using primers complimentary to the invariant seq.



108bp PCR fragments cloned into pGEM-T and sequenced. Clones with the proper sequence will be cut with 2 restriction enzymes. 4 fragments will be ligated together with pcDNA3.1 in a stepwise manner from the 5' to 3' end of gene

Fragments to be ligated with pcDNA3.1 (1-4 are in order from 5' to 3')	Restriction Enzymes Used to Cleave Fragment
Fragment 1	EcoRI/BsmBI
Fragment 2	BbsI/BsmBI
Fragment 3	BbsI/BsmBI
Fragment 4	BbsI/BamHI
pcDNA3.1	EcoRI/BamHI



Ligations will be repeated stepwise 5' to 3' until the entire gene has been cloned into pcDNA3.1

Figure 7

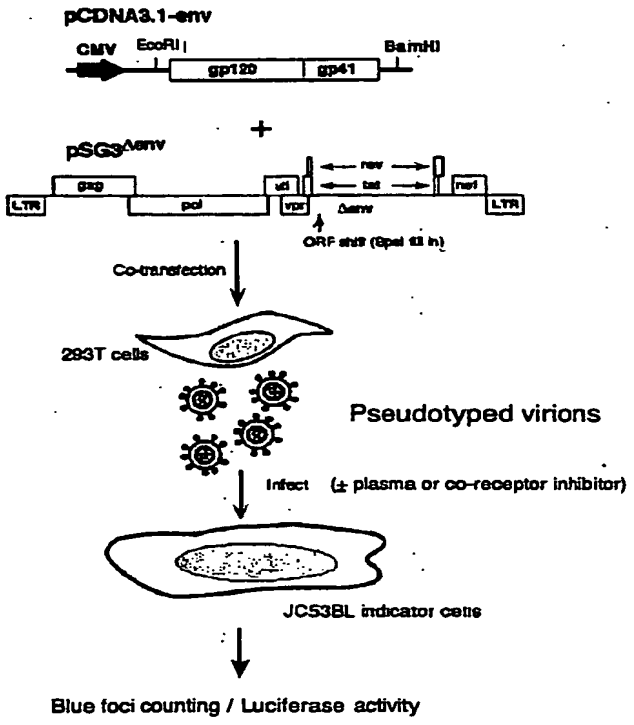
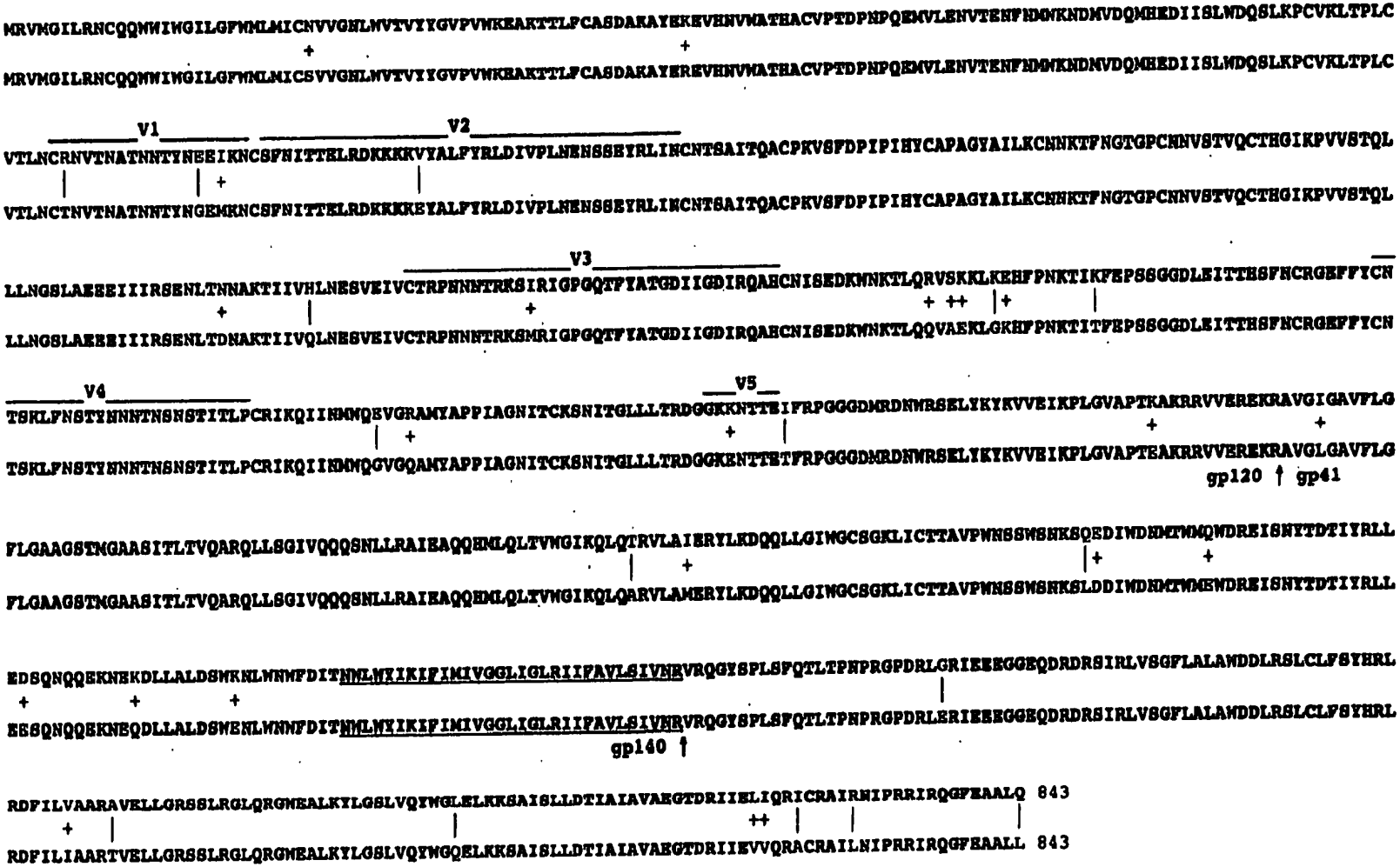

pCDNA3.1-env
CMV
EcoRI
BamHI
gp120
gp41
+
pSG3Δenv
gag
pol
vif
vpr
tat
rev
nef
LTR
LTR
Δenv
ORF shift (SpeI site in)
Co-transfection
293T cells
Pseudotyped virions
Infect (± plasma or co-receptor inhibitor)
JC53BL indicator cells
Blue foci counting / Luciferase activity

Figure 8



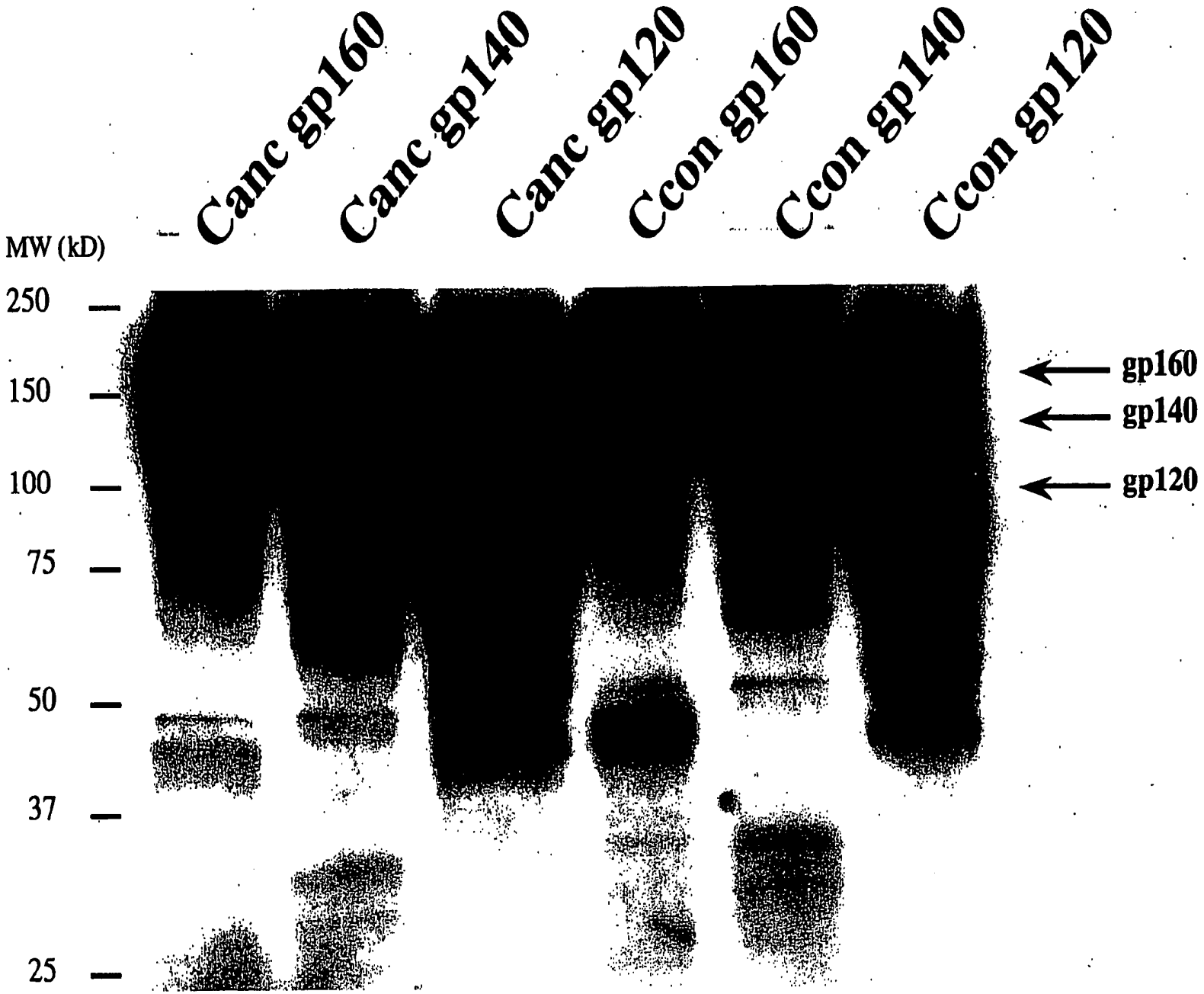

Canc gp160
Canc gp140
Canc gp120
Ccon gp160
Ccon gp140
Ccon gp120
MW (kD)
250
150
100
75
50
37
25
gp160
gp140
gp120

Figure 10 A

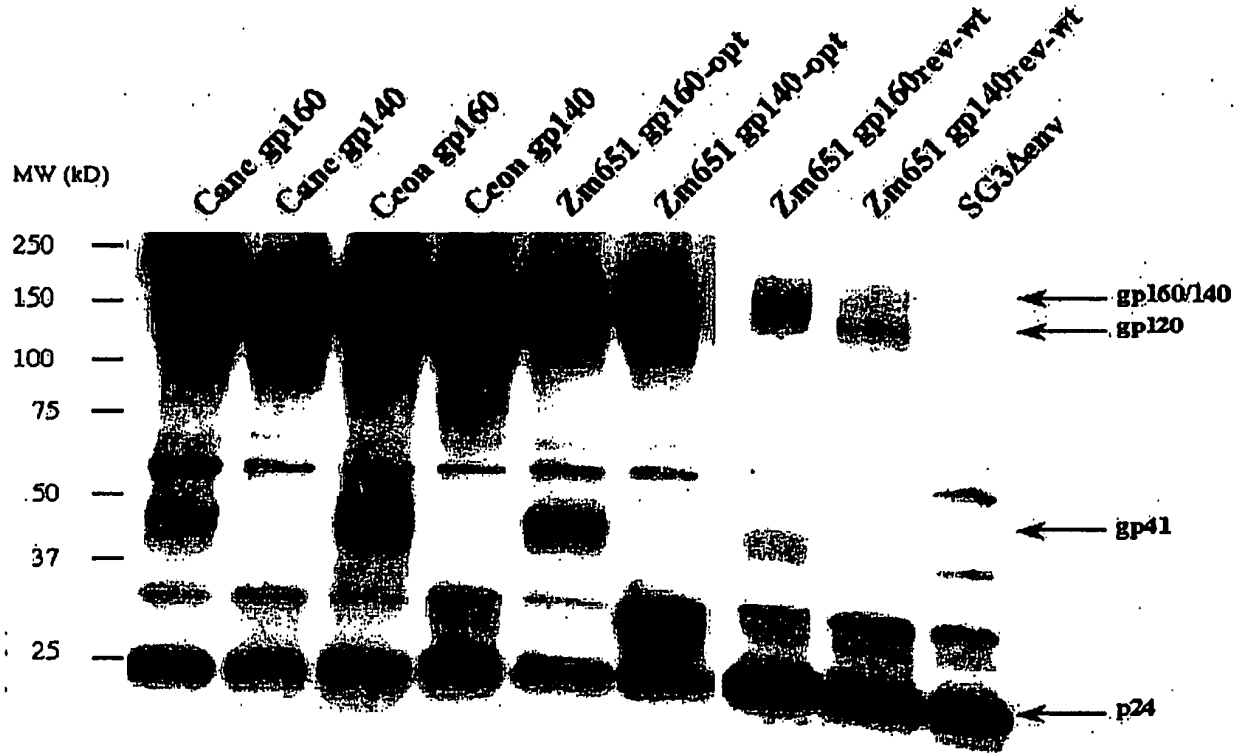

MW (kD)
Cane gp160
Cane gp140
Ccon gp160
Ccon gp140
Zm651 gp160-opt
Zm651 gp140-opt
Zm651 gp160rev-wt
Zm651 gp140rev-wt
SG3Δenv
250
150
100
75
50
37
25
gp160/140
gp120
gp41
p24

Figure 10B

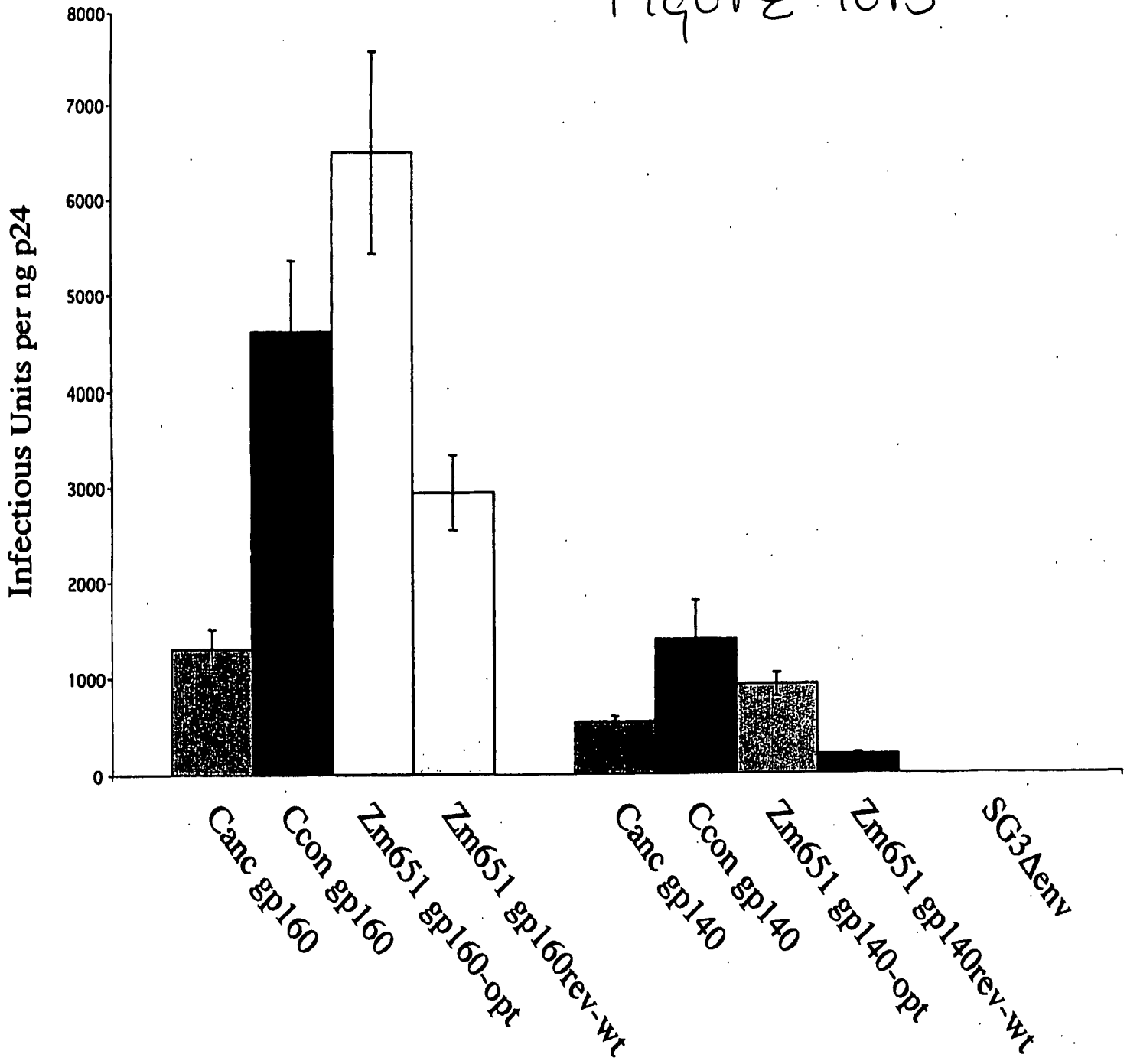

Infectious Units per ng p24
8000
7000
6000
5000
4000
3000
2000
1000
0
Canc gp160
Ccon gp160
Zm651 gp160-opt
Zm651 gp160rev-wt
Canc gp140
Ccon gp140
Zm651 gp140-opt
Zm651 gp140rev-wt
SG3Δenv

Figure 11

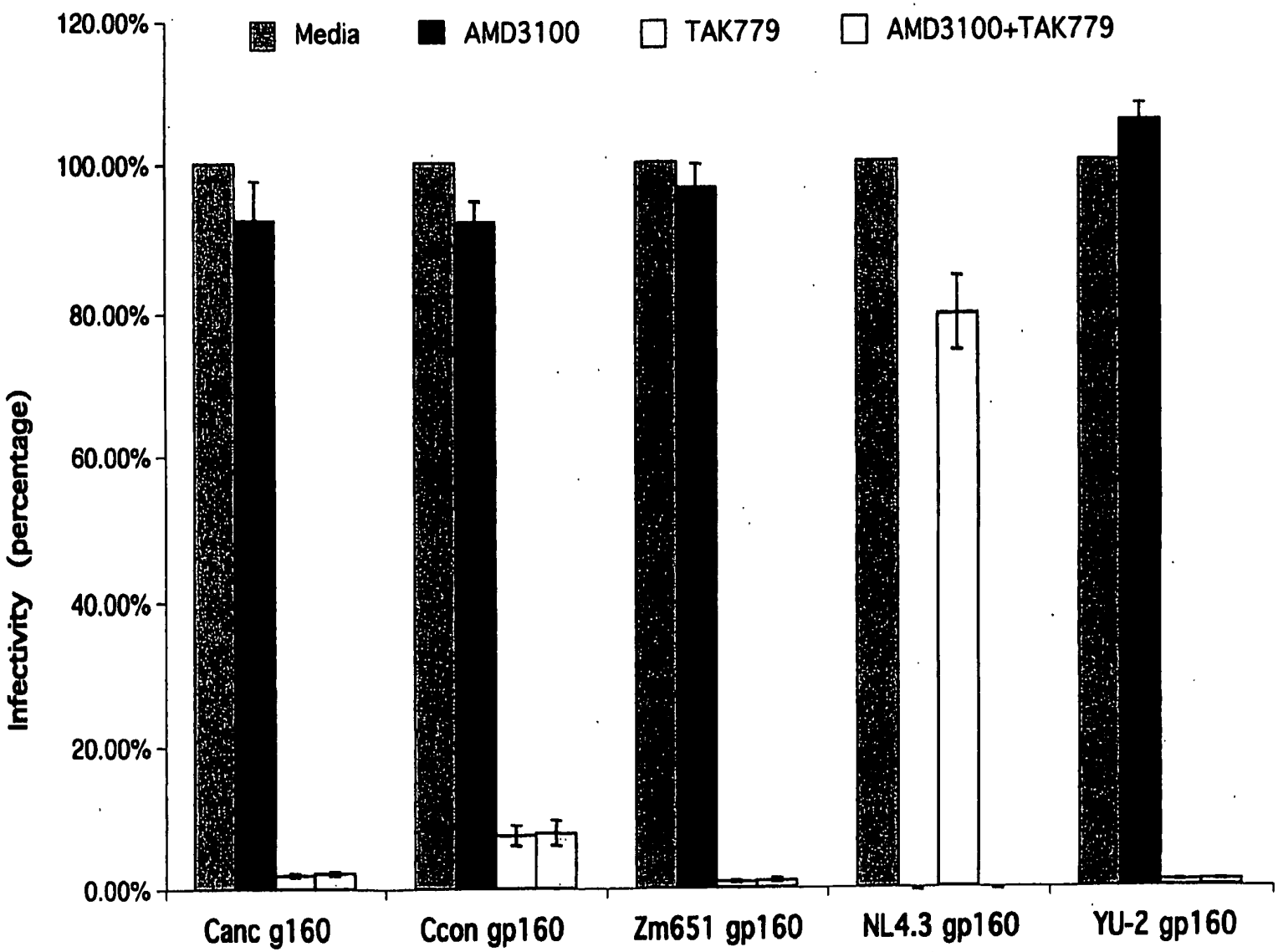

Media
AMD3100
TAK779
AMD3100+TAK779
120.00%
100.00%
80.00%
60.00%
40.00%
20.00%
0.00%
Infectivity (percentage)
Canc g160
Ccon gp160
Zm651 gp160
NL4.3 gp160
YU-2 gp160

Figure 12

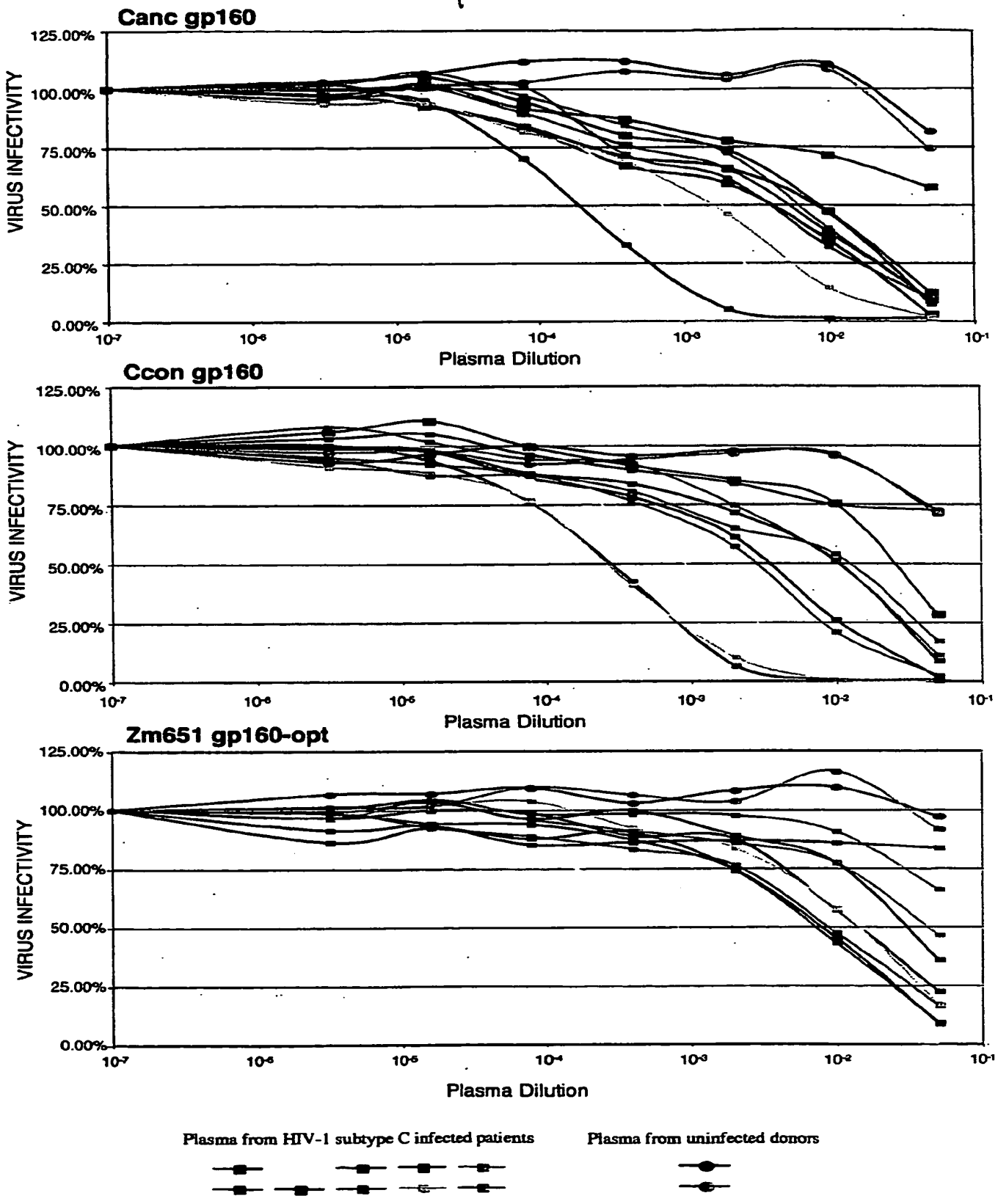

Canc gp160
125.00%
100.00%
75.00%
50.00%
25.00%
0.00%
VIRUS INFECTIVITY
10-7
10-6
10-5
10-4
10-3
10-2
10-1
Plasma Dilution
Ccon gp160
125.00%
100.00%
75.00%
50.00%
25.00%
0.00%
VIRUS INFECTIVITY
10-7
10-6
10-5
10-4
10-3
10-2
10-1
Plasma Dilution
Zm651 gp160-opt
125.00%
100.00%
75.00%
50.00%
25.00%
0.00%
VIRUS INFECTIVITY
10-7
10-6
10-5
10-4
10-3
10-2
10-1
Plasma Dilution
Plasma from HIV-1 subtype C infected patients
Plasma from uninfected donors

Figure 13

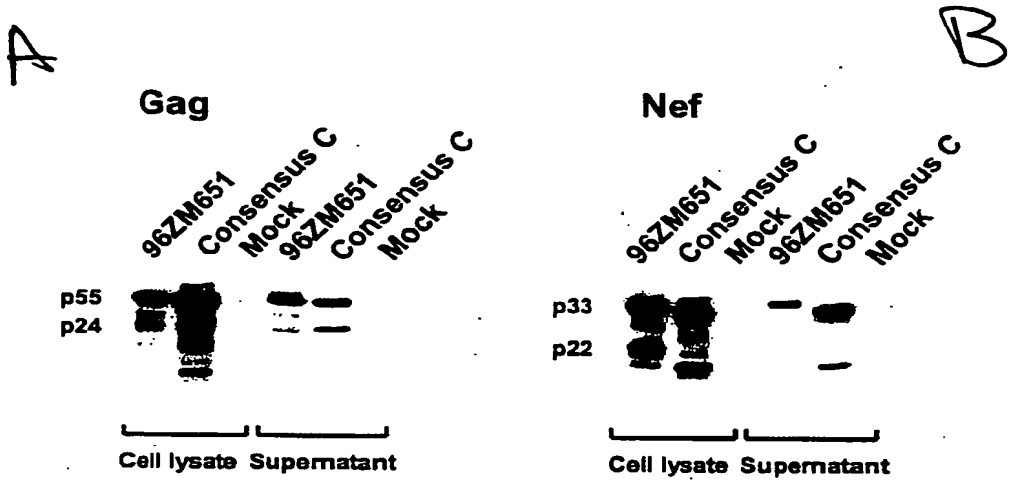

A
Gag
96ZM651
Consensus C
Mock
96ZM651
Consensus C
Mock
p55
p24
Cell lysate
Supernatant
B
Nef
96ZM651
Consensus C
Mock
96ZM651
Consensus C
Mock
p33
p22
Cell lysate
Supernatant

Figure 13C

C.con.gag (subtype C consensus gag)
MGARASILRGGKLDTWEKIRLRPGGKKRYMIKHLVWASRELERFALNPGLLETSEGCKQIMKQLQPA
LQTGTEELRSLYNTVATLYCVHEKIEVRDTKEALDKIEEEQNKSQQKTQQAEAAADGKVSQNYPI
VQNLQGQMVHQAISPRTLNAWVKVIEEKAFSPEVIPMFTALSEGATPQDLNTMLNTVGGHQAAMQMLKDT
INEEAAEWDRLHPVHAGPIAPGQMREPRGSDIAGTTSTLQEQIAWMTSNPPVPVGDIYKRWIILGLNKIV
RMYSPVSILDIKQGPKEPFRDYVDRFFKTLRAEQATQDVKNWMTDTLLVQNANPDCKTILRALGPGASLE
EMMTACQGVGGPSHKARVLAEAMSQANNTNIMMQRSNFKGPKRIVKCFNCGKEGHIARNCRAPRKKGCWK
CGKEGHQMKDCTERQANFLGKIWPSHKGRPGNFLQSRPEPTAPPAESFRFEETTPA
PKQEPKDREPLTSLKSLFGSDPLSQ

C.con.nef (subtype C consensus nef)
MGGKWSKSSIVGWPAVRERIRRTEPAAEGVGAASQDLDKYGALTSSNTATNNADCAWLEAQEEEEEV
GFPVRPQVPLRPMTYKAAFDLSFFLKEKGGLEGLIYSKKRQEILDLWVYHTQGFFPDWQNYTPGPGVRYP
LTFGWCFKLVPVDPREVEEANEGENNCLLHPMSQHGMEDEDREVLKWKFDSHLARRHMARELHPEYYKDC

Figure 13D

Figure 13E

C.con.gag (subtype C consensus gag. Not in the public domain)

GCCGCCGCCATGGGCGCCCGCGCCAGCATCCTGCGCGGCGGCAAGCTGGACACCTGGGAGAAGATCCGCC
TGCGCCCCGGCGGCAAGAAGCGCTACATGATCAAGCACCTGGTGTGGGCCAGCCGCGAGCTGGAGCGCTT
CGCCCTGAACCCCGGCCTGCTGGAGACCAGCGAGGGCTGCAAGCAGATCATGAAGCAGCTGCAGCCCGCC
CTGCAGACCGGCACCGAGGAGCTGCGCAGCCTGTACAACACCGTGGCCACCCTGTACTGCGTGCACGAGA
AGATCGAGGTGCGCGACACCAAGGAGGCCCTGGACAAGATCGAGGAGGAGCAGAACAAGAGCCAGCAGAA
GACCCAGCAGGCCGAGGCCGCCGCCGACGGCAAGGTGAGCCAGAACTACCCCATCGTGCAGAACCTGCAG
GGCCAGATGGTGCACCAGGCCATCAGCCCCCGCACCCTGAACGCCTGGGTGAAGGTGATCGAGGAGAAGG
CCTTCAGCCCCGAGGTGATCCCCATGTTCACCGCCCTGAGCGAGGGCGCCACCCCCCAGGACCTGAACAC
CATGCTGAACACCGTGGGCGGCCACCAGGCCGCCATGCAGATGCTGAAGGACACCATCAACGAGGAGGCC
GCCGAGTGGGACCGCCTGCACCCCGTGCACGCCGGCCCCATCGCCCCCGGCCAGATGCGCGAGCCCCGCG
GCAGCGACATCGCCGGCACCACCAGCACCCTGCAGGAGCAGATCGCCTGGATGACCAGCAACCCCCCCGT
GCCCGTGGGCGACATCTACAAGCGCTGGATCATCCTGGGCCTGAACAAGATCGTGCGCATGTACAGCCCC
GTGAGCATCCTGGACATCAAGCAGGGCCCCAAGGAGCCCTTCCGCGACTACGTGGACCGCTTCTTCAAGA
CCCTGCGCGCCGAGCAGGCCACCCAGGACGTGAAGAACTGGATGACCGACACCCTGCTGGTGCAGAACGC
CAACCCCGACTGCAAGACCATCCTGCGCGCCCTGGGCCCCGGCGCCAGCCTGGAGGAGATGATGACCGCC
TGCCAGGGCGTGGGCGGCCCCAGCCACAAGGCCCGCGTGCTGGCCGAGGCCATGAGCCAGGCCAACAACA
CCAACATCATGATGCAGCGCAGCAACTTCAAGGGCCCCAAGCGCATCGTGAAGTGCTTCAACTGCGGCAA
GGAGGGCCACATCGCCCGCAACTGCCGCGCCCCCCGCAAGAAGGGCTGCTGGAAGTGCGGCAAGGAGGGC
CACCAGATGAAGGACTGCACCGAGCGCCAGGCCAACTTCCTGGGCAAGATCTGGCCCAGCCACAAGGGCC
GCCCCGGCAACTTCCTGCAGAGCCGCCCCGAGCCCACCGCCCCCCCCCGCCGAGAGCTTCCGCTTCGAGGA
GACCACCCCCGCCCCCAAGCAGGAGCCCAAGGACCGCGAGCCCCTGACCAGCCTGAAGAGCCTGTTCGGC
AGCGACCCCCTGAGCCAGTAA

C.con.nef (subtype C consensus nef. Not in the public domain)

GCCGCCGCCATGGGCGGCAAGTGGAGCAAGAGCAGCATCGTGGGCTGGCCCGCCGTGCGCGAGCGCATCC
GCCGCACCGAGCCCGCCGCCGAGGGCGTGGGCGCCGCCAGCCAGGACCTGGACAAGTACGGCGCCCTGAC
CAGCAGCAACACCGCCACCAACAACGCCGACTGCGCCTGGCTGGAGGCCCAGGAGGAGGAGGAGGAGGTG
GGCTTCCCCGTGCGCCCCCAGGTGCCCCTGCGCCCCATGACCTACAAGGCCGCCTTCGACCTGAGCTTCT
TCCTGAAGGAGAAGGGCGGCCTGGAGGGCCTGATCTACAGCAAGAAGCGCCAGGAGATCCTGGACCTGTG
GGTGTACCACACCCAGGGCTTCTTCCCCGACTGGCAGAACTACACCCCCGGCCCCGGCGTGCGCTACCCC
CTGACCTTCGGCTGGTGCTTCAAGCTGGTGCCCGTGGACCCCCGCGAGGTGGAGGAGGCCAACGAGGGCG
AGAACAACTGCCTGCTGCACCCCATGAGCCAGCACGGCATGGAGGACGAGGACCGCGAGGTGCTGAAGTG
GAAGTTCGACAGCCACCTGGCCCGCCGCCACATGGCCCGCGAGCTGCACCCCGAGTACTACAAGGACTGC
TGA

Figure 13F

Figure 14A

CONs.env (group M consensus env gene. This one contain the consensus sequence for variable regions in env gene)
MRVRGIQRNCQHLWRWGTLILGMLMICSAAENLWVTVYYGVPVWKEANTTLFCASDAKAYDTEVHNV
WATHACVPTDPNPQEIVLENVTENFNMWKNNMVEQMHEDIISLWDQSLKPCVKLTPLCVTLNCTNVNVTN
TTNNTEEKGEIKNCSFNITTEIRDKKQKVYALFYRLDVVPIDDNNNNSSNYRLINCNTSAITQACPKVSF
EPIPIHYCAPAGFAILKCNDKKFNGTGPCKNVSTVQCTHGIKPVVSTQLLLNGSLAEEEIIIRSENITNN
AKTIIVQLNESVEINCTRPNNNTRKSIRIGPGQAFYATGDIIGDIRQAHCNISGTKWNKTLQQVAKKLRE
HFNNKTIIFKPSSGGDLEITTHSFNCRGEFFYCNTSGLFNSTWIGNGTKNNNNTNDTITLPCRIKQIINM
WQGVGQAMYAPPIEGKITCKSNITGLLLTRDGGNNNTNETEIFRPGGGDMRDNWRSELYKYKVVKIEPLG
VAPTKAKRRVVEREKRAVGIGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLRAIEAQQHL
LQLTVWGIKQLQARVLAVERYLKDQQLLGIWGCSGKLICTTTVPWNSSWSNKSQDEIWDNMTWMEWEREI
NNYTDIIYSLIEESQNQQEKNEQELLALDKWASLWNWFDITNWLWYIKIFIMIVGGLIGLRIVFAVLSIV
NRVRQGYSPLSFQTLIPNPRGPDRPEGIEEEGGEQDRDRSIRLVNGFLALAWDDLRSLCLFSYHRLRDFI
LIAARTVELLGRKGLRRGWEALKYLWNLLQYWGQELKNSAISLLDTTAIAVAEGTDRVIEVVQRACRAIL
NIPRRIRQGLERALL

Figure 14B

CONs.env (gorup M consensus env gene. This one contain the consensus sequence for variable regions in env gene. The identical amino acid sequences as in the public domain)

GCCGCCGCCATGCGCGTGCGCGGCATCCAGCGCAACTGCCAGCACCTGTG
GCGCTGGGGCACCCTGATCCTGGGCATGCTGATGATCTGCTCCGCCGCCG
AGAACCTGTGGGTGACCGTGTACTACGGCGTGCCCGTGTGGAAGGAGGCC
AACACCACCCTGTTCTGCGCCTCCGACGCCAAGGCCTACGACACCGAGGT
GCACAACGTGTGGGCCACCCACGCCTGCGTGCCCACCGACCCCAACCCCC
AGGAGATCGTGCTGGAGAACGTGACCGAGAACTTCAACATGTGGAAGAAC
AACATGGTGGAGCAGATGCACGAGGACATCATCTCCCTGTGGGACCAGTC
CCTGAAGCCCTGCGTGAAGCTGACCCCCCTGTGCGTGACCCTGAACTGCA
CCAACGTGAACGTGACCAACACCACCAACAACACCGAGGAGAAGGGCGAG
ATCAAGAACTGCTCCTTCAACATCACCACCGAGATCCGCGACAAGAAGCA
GAAGGTGTACGCCCTGTTCTACCGCCTGGACGTGGTGCCCATCGACGACA
ACAACAACAACTCCTCCAACTACCGCCTGATCAACTGCAACACCTCCGCC
ATCACCCAGGCCTGCCCCAAGGTGTCCTTCGAGCCCATCCCCATCCACTA
CTGCGCCCCCGCCGGCTTCGCCATCCTGAAGTGCAACGACAAGAAGTTCA
ACGGCACCGGCCCCTGCAAGAACGTGTCCACCGTGCAGTGCACCCACGGC
ATCAAGCCCGTGGTGTCCACCCAGCTGCTGCTGAACGGCTCCCTGGCCGA
GGAGGAGATCATCATCCGCTCCGAGAACATCACCAACAACGCCAAGACCA
TCATCGTGCAGCTGAACGAGTCCGTGGAGATCAACTGCACCCGCCCCAAC
AACAACACCCGCAAGTCCATCCGCATCGGCCCCGGCCAGGCCTTCTACGC
CACCGGCGACATCATCGGCGACATCCGCCAGGCCCACTGCAACATCTCCG
GCACCAAGTGGAACAAGACCCTGCAGCAGGTGGCCAAGAAGCTGCGCGAG
CACTTCAACAACAAGACCATCATCTTCAAGCCCTCCTCCGGCGGCGACCT
GGAGATCACCACCCACTCCTTCAACTGCCGCGGCGAGTTCTTCTACTGCA
ACACCTCCGGCCTGTTCAACTCCACCTGGATCGGCAACGGCACCAAGAAC
AACAACAACACCAACGACACCATCACCCTGCCCTGCCGCATCAAGCAGAT
CATCAACATGTGGCAGGGCGTGGGCCAGGCCATGTACGCCCCCCCCATCG
AGGGCAAGATCACCTGCAAGTCCAACATCACCGGCCTGCTGCTGACCCGC
GACGGCGGCAACAACAACACCAACGAGACCGAGATCTTCCGCCCCGGCGG
CGGCGACATGCGCGACAACTGGCGCTCCGAGCTGTACAAGTACAAGGTGG
TGAAGATCGAGCCCCTGGGCGTGGCCCCCACCAAGGCCAAGCGCCGCGTG
GTGGAGCGCGAGAAGCGCGCCGTGGGCATCGGCGCCGTGTTCCTGGGCTT
CCTGGGCGCCGCCGGCTCCACCATGGGCGCCGCCTCCATCACCCTGACCG
TGCAGGCCCGCCAGCTGCTGTCCGGCATCGTGCAGCAGCAGTCCAACCTG
CTGCGCGCCATCGAGGCCCAGCAGCACCTGCTGCAGCTGACCGTGTGGGG
CATCAAGCAGCTGCAGGCCCGCGTGCTGGCCGTGGAGCGCTACCTGAAGG
ACCAGCAGCTGCTGGGCATCTGGGGCTGCTCCGGCAAGCTGATCTGCACC
ACCACCGTGCCCTGGAACTCCTCCTGGTCCAACAAGTCCCAGGACGAGAT
CTGGGACAACATGACCTGGATGGAGTGGGAGCGCGAGATCAACAACTACA
CCGACATCATCTACTCCCTGATCGAGGAGTCCCAGAACCAGCAGGAGAAG
AACGAGCAGGAGCTGCTGGCCCTGGACAAGTGGGCCTCCCTGTGGAACTG
GTTCGACATCACCAACTGGCTGTGGTACATCAAGATCTTCATCATGATCG
TGGGCGGCCTGATCGGCCTGCGCATCGTGTTCGCCGTGCTGTCCATCGTG
AACCGCGTGCGCCAGGGCTACTCCCCCCTGTCCTTCCAGACCCTGATCCC
CAACCCCCGCCGGCCCCGACCGCCCCGAGGGCATCGAGGAGGAGGGCGGCG
AGCAGGACCGCGACCGCTCCATCCGCCTGGTGAACGGCTTCCTGGCCCTG
GCCTGGGACGACCTGCGCTCCCTGTGCCTGTTCTCCTACCACCGCCTGCG
CGACTTCATCCTGATCGCCGCCCGCACCGTGGAGCTGCTGGGCCGCAAGG
GCCTGCGCCGCGGCTGGGAGGCCCTGAAGTACCTGTGGAACCTGCTGCAG
TACTGGGGCCAGGAGCTGAAGAACTCCGCCATCTCCCTGCTGGACACCAC
CGCCATCGCCGTGGCCGAGGGCACCGACCGCGTGATCGAGGTGGTGCAGC
GCGCCTGCCGCGCCATCCTGAACATCCCCCGCCGCATCCGCCAGGGCCTG
GAGCGCGCCCTGCTGTAA

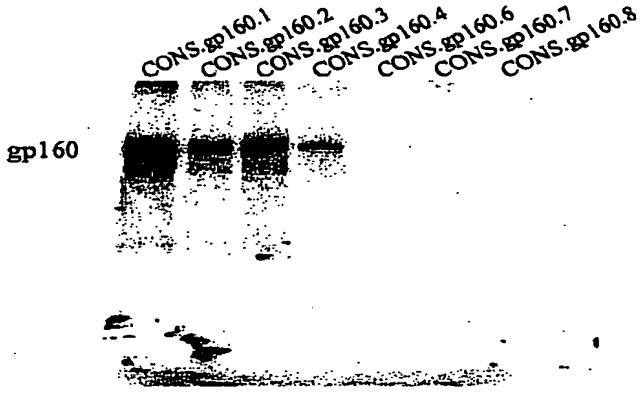
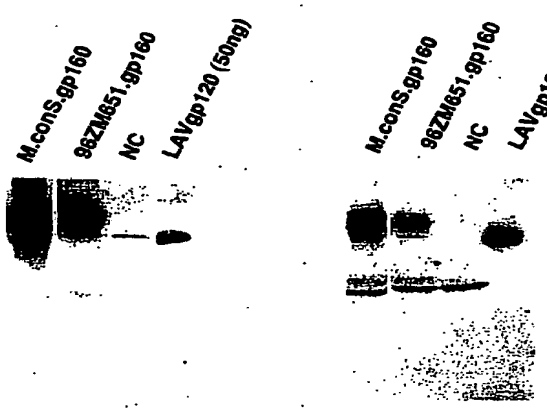

CONS.gp160.1
CONS.gp160.2
CONS.gp160.3
CONS.gp160.4
CONS.gp160.6
CONS.gp160.7
CONS.gp160.8
gp160

Figure 14C

Figure 15

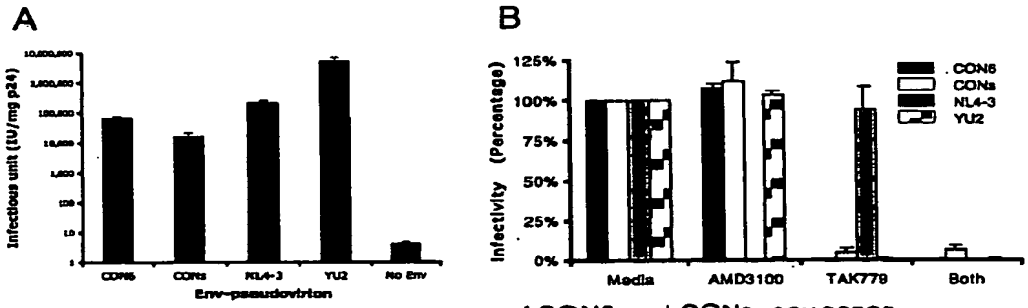
A



B

Cell lysate **Supernatant**

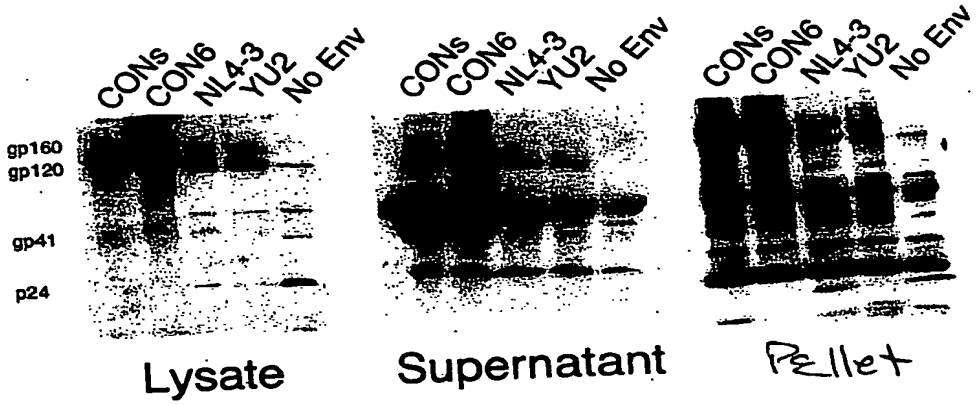
Expression of CONs *env* gene in mammalian cells



Infectivity and coreceptor usage of CON6 and CONs *env* genes

Figure 16

A B C



Env protein incorporation in CON6 and CONs Env-pseudovirions

Figure 17

Figure 18A

A.con.env (subtype A consensus env)
MRVMGIQRNCQHLWRWGTMILGMIIICSAAENLWVTVYYGVPVWKDAETTLFCASDAKAYDTEVHNV
WATHACVPTDPNPQEINLENVTEEFNMWKNNMVEQMHTDIISLWDQSLKPCVKLTPLCVTLNCSNVNVTT
NITNITDNMKGEIKNCSFNMTTELRDKKQKVYSLFYKLDVVQINKSNSSSQYRLINCNTSAITQACPKVS
FEPIPIHYCAPAGFAILKCKDKEFNGTGPCKNVSTVQCTHGIKPVVSTQLLLNGSLAEEEVMIRSENITN
NAKNIIVQLTKPVKINCTRPNNNTRKSIRIGPGQAFYATGDIIGDIRQAHCNVSRTEWNETLQKVAKQLR
KYFNNKTIIFTNSSGGDLEITTHSFNCGGEFFYCNTSGLFNSTWNGNGTKKKNSTESNDTITLPCRIKQI
INMWQRVGQAMYAPPIQGVIRCESNITGLLLTRDGGDNNSKNETFRPGGGDMRDNWRSELYKYKVVKIEP
LGVAPTKAKRRVVEREKRAVGIGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLRAIEAQQ
HLLKLTVWGIKQLQARVLAVERYLKDQQLLGIWGCSGKLICTTNVPWNSSWSNKSQSEIWDNMTWLQWDK
EISNYTDIIYNLIEESQNQQEKNEQDLLALDKWANLWNWFDISNWLWYIKIFIMIVGGLIGLRIVFAVLS
VINRVRQGYSPLSFQTHTPNPGGLDRPGRIEEEGGEQGRDRSIRLVSGFLALAWDDLRSLCLFSYHRLRD
FILIAARTVELLGHSSLKGLRLGWEGLKYLWNLLLYWGRELKISAINLLDTIAIAVAGWTDRVIEIGQRI
CRAILNIPRRIRQGLERALL

Figure 18B

A.con.env (subtype A consensus env. Identical amino acid sequence to that in the public domain)

GCCGCCGCCATGCGCGTGATGGGCATCCAGCGCAACTGCCAGCACCTGTG
GCGCTGGGGCACCATGATCCTGGGCATGATCATCATCTGCTCCGCCGCCG
AGAACCTGTGGGTGACCGTGTACTACGGCGTGCCCGTGTGGAAGGACGCC
GAGACCACCCTGTTCTGCGCCTCCGACGCCAAGGCCTACGACACCGAGGT
GCACAACGTGTGGGCCACCCACGCCTGCGTGCCCACCGACCCCAACCCCC
AGGAGATCAACCTGGAGAACGTGACCGAGGAGTTCAACATGTGGAAGAAC
AACATGGTGGAGCAGATGCACACCGACATCATCTCCCTGTGGGACCAGTC
CCTGAAGCCCTGCGTGAAGCTGACCCCCCTGTGCGTGACCCTGAACTGCT
CCAACGTGAACGTGACCACCAACATCACCAACATCACCGACAACATGAAG
GGCGAGATCAAGAACTGCTCCTTCAACATGACCACCGAGCTGCGCGACAA
GAAGCAGAAGGTGTACTCCCTGTTCTACAAGCTGGACGTGGTGCAGATCA
ACAAGTCCAACTCCTCCTCCCAGTACCGCCTGATCAACTGCAACACCTCC
GCCATCACCCAGGCCTGCCCCAAGGTGTCCTTCGAGCCCATCCCCATCCA
CTACTGCGCCCCCCGCCGGCTTCGCCATCCTGAAGTGCAAGGACAAGGAGT
TCAACGGCACCGGCCCCTGCAAGAACGTGTCCACCGTGCAGTGCACCCAC
GGCATCAAGCCCGTGGTGTCCACCCAGCTGCTGCTGAACGGCTCCCTGGC
CGAGGAGGAGGTGATGATCCGCTCCGAGAACATCACCAACAACGCCAAGA
ACATCATCGTGCAGCTGACCAAGCCCGTGAAGATCAACTGCACCCGCCCC
AACAACAACACCCGCAAGTCCATCCGCATCGGCCCCGGCCAGGCCTTCTA
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CCCGCACCGAGTGGAACGAGACCCTGCAGAAGGTGGCCAAGCAGCTGCGC
AAGTACTTCAACAACAAGACCATCATCTTCACCAACTCCTCCGGCGGCGA
CCTGGAGATCACCACCCACTCCTTCAACTGCGGCGGCGAGTTCTTCTACT
GCAACACCTCCGGCCTGTTCAACTCCACCTGGAACGGCAACGGCACCAAG
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CAAGCAGATCATCAACATGTGGCAGCGCGTGGGCCAGGCCATGTACGCCC
CCCCCATCCAGGGCGTGATCCGCTGCGAGTCCAACATCACCGGCCTGCTG
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CGCGTGGTGGAGCGCGAGAAGCGCGCCGTGGGCATCGGCGCCGTGTTCCT
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GTGGGGCATCAAGCAGCTGCAGGCCCGCGTGCTGGCCGTGGAGCGCTACC
TGAAGGACCAGCAGCTGCTGGGCATCTGGGGCTGCTCCGGCAAGCTGATC
TGCACCACCAACGTGCCCTGGAACTCCTCCTGGTCCAACAAGTCCCAGTC
CGAGATCTGGGACAACATGACCTGGCTGCAGTGGGACAAGGAGATCTCCA
ACTACACCGACATCATCTACAACCTGATCGAGGAGTCCCAGAACCAGCAG
GAGAAGAACGAGCAGGACCTGCTGGCCCTGGACAAGTGGGCCAACCTGTG
GAACTGGTTCGACATCTCCAACTGGCTGTGGTACATCAAGATCTTCATCA
TGATCGTGGGCGGCCTGATCGGCCTGCGCATCGTGTTCGCCGTGCTGTCC
GTGATCAACCGCGTGCGCCAGGGCTACTCCCCCCTGTCCTTCCAGACCCA
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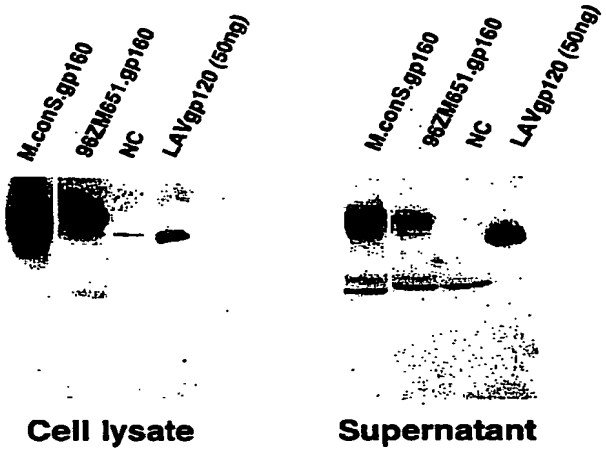
CCTGCGCGACTTCATCCTGATCGCCGCCCGCACCGTGGAGCTGCTGGGCC
ACTCCTCCCTGAAGGGCCTGCGCCTGGGCTGGGAGGGCCTGAAGTACCTG
TGGAACCTGCTGCTGTACTGGGGCCGCGAGCTGAAGATCTCCGCCATCAA
CCTGCTGGACACCATCGCCATCGCCGTGGCCGGCTGGACCGACCGCGTGA
TCGAGATCGGCCAGCGCATCTGCCGCGCCATCCTGAACATCCCCCGCCGC
ATCCGCCAGGGCCTGGAGCGCGCCCTGCTGTAA

C D



Expression of A.con *env* gene in mammalian cells

Figure 18

Figure 19A

M.con.gag (group M consensus gag. Identical amino acid sequence to that in the public domain)

GCCGCCGCCATGGGCGCCCGCGCCTCCGTGCTGTCCGGCGGCAAGCTGGA
CGCCTGGGAGAAGATCCGCCTGCGCCCCGGCGGCAAGAAGAAGTACCGCC
TGAAGCACCTGGTGTGGGCCTCCCGCGAGCTGGAGCGCTTCGCCCTGAAC
CCCGGCCTGCTGGAGACCTCCGAGGGCTGCAAGCAGATCATCGGCCAGCT
GCAGCCCGCCCTGCAGACCGGCTCCGAGGAGCTGCGCTCCCTGTACAACA
CCGTGGCCACCCTGTACTGCGTGCACCAGCGCATCGAGGTGAAGGACACC
AAGGAGGCCCTGGAGAAGATCGAGGAGGAGCAGAACAAGTCCCAGCAGAA
GACCCAGCAGGCCGCCGCCGACAAGGGCAACTCCTCCAAGGTGTCCCAGA
ACTACCCCATCGTGCAGAACCTGCAGGGCCAGATGGTGCACCAGGCCATC
TCCCCCCGCACCCTGAACGCCTGGGTGAAGGTGATCGAGGAGAAGGCCTT
CTCCCCCGAGGTGATCCCCATGTTCTCCGCCCTGTCCGAGGGCGCCACCC
CCCAGGACCTGAACACCATGCTGAACACCGTGGGCGGCCACCAGGCCGCC
ATGCAGATGCTGAAGGACACCATCAACGAGGAGGCCGCCGAGTGGGACCG
CCTGCACCCCGTGCACGCCGGCCCCATCCCCCCCGGCCAGATGCGCGAGC
CCCGCGGCTCCGACATCGCCGGCACCACCTCCACCCTGCAGGAGCAGATC
GCCTGGATGACCTCCAACCCCCCCCATCCCCGTGGGCGAGATCTACAAGCG
CTGGATCATCCTGGGCCTGAACAAGATCGTGCGCATGTACTCCCCCGTGT
CCATCCTGGACATCCGCCAGGGCCCCAAGGAGCCCTTCCGCGACTACGTG
GACCGCTTCTTCAAGACCCTGCGCGCCGAGCAGGCCACCCAGGACGTGAA
GAACTGGATGACCGACACCCTGCTGGTGCAGAACGCCAACCCCGACTGCA
AGACCATCCTGAAGGCCCTGGGCCCCGGCGCCACCCTGGAGGAGATGATG
ACCGCCTGCCAGGGCGTGGGCGGCCCCGGCCACAAGGCCCGCGTGCTGGC
CGAGGCCATGTCCCAGGTGACCAACGCCGCCATCATGATGCAGCGCGGCA
ACTTCAAGGGCCAGCGCCGCATCATCAAGTGCTTCAACTGCGGCAAGGAG
GGCCACATCGCCCGCAACTGCCGCGCCCCCCGCAAGAAGGGCTGCTGGAA
GTGCGGCAAGGAGGGCCACCAGATGAAGGACTGCACCGAGCGCCAGGCCA
ACTTCCTGGGCAAGATCTGGCCCTCCAACAAGGGCCGCCCCGGCAACTTC
CTGCAGTCCCGCCCCGAGCCCACCGCCCCCCCCGCCGAGTCCTTCGGCTT
CGGCGAGGAGATCACCCCCTCCCCCAAGCAGGAGCCCAAGGACAAGGAGC
CCCCCCTGACCTCCCTGAAGTCCCTGTTCGGCAACGACCCCCTGTCCCAG
TAA

Figure 19B

M.con.pol.nuc

GCCGCCGCCatgccccagatcaccctgtggcagcgccccctggtgaccat
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acaagcgcacccaggacttctgggaggtgcagctgggcatcccccacccc
gccggcctgaagaagaagaagtccgtgaccgtgctggacgtgggcgacgc
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agcagggccaggaccagtggacctaccagatctaccaggagcccttcaag
aacctcaagaccggcaagtacgccaagatgcgctccgcccacaccaacga
cgtgaagcagctgaccgaggccgtgcagaagatcgccaccgagtccatcg
tgatctggggcaagaccccaagttccgcctgcccatccagaaggagacc

Figure 19B
continued

tgggagacctggtggaccgagtactggcaggccacctggattcccgagtg
ggagttcgtgaacacccccccctggtgaagctgtggtaccagctggaga
aggagcccatcgccggcgccgagaccttctacgtggacggcgccgccaac
cgcgagaccaagctgggcaaggccggctacgtgaccgaccgcggccgcca
gaaggtggtgtccctgaccgagaccaccaaccagaaaaccgagctgcagg
ccatccacctggccctgcaggactccggctccgaggtgaacatcgtgacc
gactcccagtacgccctgggcatcatccaggcccagcccgacaagtccga
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cccgccaagctgctgtggaagggcgagggcgccgtggtgatccaggacaa
ctccgacatcaaggtggtgccccgccgcaaggccaagatcatccgcgact
acggcaagcagatggccggcgacgactgcgtggccggccgccaggacgag
gacTAA

Figure 19C

M.con.nef (group M consensus nef. Identical amino acid sequence to that in the public domain)
GCCGCCGCCATGGGCGGCAAGTGGTCCAAGTCCTCCATCGTGGGCTGGCC
CGCCGTGCGCGAGCGCATCCGCCGCACCCACCCCGCCGCCGAGGGCGTGG
GCGCCGTGTCCCAGGACCTGGACAAGCACGGCGCCATCACCTCCTCCAAC
ACCGCCGCCAACAACCCCGACTGCGCCTGGCTGGAGGCCCAGGAGGAGGA
GGAGGAGGTGGGCTTCCCCGTGCGCCCCCAGGTGCCCCTGCGCCCCATGA
CCTACAAGGCCGCCCTGGACCTGTCCCACTTCCTGAAGGAGAAGGGCGGC
CTGGAGGGCCTGATCTACTCCAAGAAGCGCCAGGAGATCCTGGACCTGTG
GGTGTACCACACCCAGGGCTACTTCCCCGACTGGCAGAACTACACCCCCG
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CCCGTGGACCCCGAGGAGGTGGAGGAGGCCAACGAGGGCGAGAACAACTC
CCTGCTGCACCCCATGTGCCAGCACGGCATGGAGGACGAGGAGCGCGAGG
TGCTGATGTGGAAGTTCGACTCCCGCCTGGCCCTGCGCCACATCGCCCGC
GAGCTGCACCCCGAGTACTACAAGGACTGCTAA

FIGURE 19D

C.con.pol.nuc

GCCGCCGCCatgccccagatcaccctgtggcagcgccccctggtgtccat
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Figure 19D
continued

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gacTAA

Figure 19E

M.con.gag (group M consensus gag)
MGARASVLSGGKLDAWEKIRLRPGGKKKYRLKHLVWASRELERFALNPGLLETSEGCKQIIGQLQPA
LQTGSEELRSLYNTVATLYCVHQRIEVKDTKEALEKIEEEQNKSQQKTQQAAADKGNSSKVSQNYPIVQN
LQGQMVHQAISPRTLNAWVKVIEEKAFSPEVIPMFSALSEGATPQDLNTMLNTVGGHQAAMQMLKDTINE
EAAEWDRLHPVHAGPIPPGQMREPRGSDIAGTTSTLQEQIAWMTSNPPIPVGEIYKRWIILGLNKIVRMY
SPVSILDIRQGPKEPFRDYVDRFFKTLRAEQATQDVKNWMTDTLLVQNANPDCKTILKALGPGATLEEMM
TACQGVGGPGHKARVLAEAMSQVTNAAIMMQRGNFKGQRRIIKCFNCGKEGHIARNCRAPRKKGCWKCGK
EGHQMKDCTERQANFLGKIWPSNKGRPGNFLQSRPEPTAPPAESFGFGEEITPSPKQEPKDKEPPLTSLK
SLFGNDPLSQ

Figure 19F

M.con.pol (group M consensus pol)
MPQITLWQRPLVTIKIGGQLKEALLaTGADDTVLEEINLPGKWKPKMIGGIGGFIKVRQYDQILIEICGK
KAIGTVLVGPTPVNIIGRNMLTQIGCTLNFPISPIETVPVKLKPGMDGPKVKQWPLTEEKIKALTEICTE
MEKEGKISKIGPENPYNTPIFAIKKKDSTKWRKLVDFRELNKRTQDFWEVQLGIPHPAGLKKKKSVTVLD
VGDAYFSVPLDEDFRKYTAFTIPSINNETPGIRYQYNVLPQGWKGSPAIFQSSMTKILEPFRTQNPEIVI
YQYMDDLYVGSDLEIGQHRAKIEELREHLLRWGFTTPDKKHQKEPPFLWMGYELHPDKWTVQPIQLPEKD
SWTVNDIQKLVGKLNWASQIYPGIKVKQLCKLLRGAKALTDIVPLTEEAELELAENREILKEPVHGVYYD
PSKDLIAEIQKQGQDQWTYQIYQEPFKNLKTGKYAKMRSAHTNDVKQLTEAVQKIATESIVIWGKTPKFR
LPIQKETWETWWTEYWQATWIPEWEFVNTPPLVKLWYQLEKEPIAGAETFYVDGAANRETKLGKAGYVTD
RGRQKVVSLTETTNQKTELQAIHLALQDSGSEVNIVTDSQYALGIIQAQPDKSESELVNQIIEQLIKKEK
VYLSWVPAHKGIGGNEQVDKLVSTGIRKVLFLDGIDKAQEEHEKYHSNWRAMASDFNLPPIVAKEIVASC
DKCQLKGEAMHGQVDCSPGIWQLDCTHLEGKIILVAVHVASGYIEAEVIPAETGQETAYFILKLAGRWPV
KVIHTDNGSNFTSAAVKAACWWAGIQQEFGIPYNPQSQGVVESMNKELKKIIGQVRDQAEHLKTAVQMAV
FIHNFKRKGGIGGYSAGERIIDIIATDIQTKELQKQITKIQNFRVYYRDSRDPIWKGPAKLLWKGEGAVV
IQDNSDIKVVPRRKAKIIRDYGKQMAGDDCVAGRQDED

Figure 19G

M.con.nef (group M consensus nef)
MGGKWSKSSIVGWPAVRERIRRTHPAAEGVGAVSQDLDKHGAITSSNTAANNPDCAWLEAQEEEEEVGFP
VRPQVPLRPMTYKAALDLSHFLKEKGGLEGLIYSKKRQEILDLWVYHTQGYFPDWQNYTPGPGIRYPLTF
GWCFKLVPVDPEEVEEANEGENNSLLHPMCQHGMEDEEREVLMWKFDSRLALRHIARELHPEYYKDC

Figure 19H

C.con.pol (subtype C consensus pol)
MPQITLWQRPLVSIKVGGQIKEALLaTGADDTVLEEINLPGKWKPKMIGGIGGFIKVRQYDQILIEICGK
KAIGTVLVGPTPVNIIGRNMLTQLGCTLNFPISPIETVPVKLKPGMDGPKVKQWPLTEEKIKALTAICEE
MEKEGKITKIGPENPYNTPVFAIKKKDSTKWRKLVDFRELNKRTQDFWEVQLGIPHPAGLKKKKSVTVLD
VGDAYFSVPLDEGFRKYTAFTIPSINNETPGIRYQYNVLPQGWKGSPAIFQSSMTKILEPFRAQNPEIVI
YQYMDDLYVGSDLEIGQHRAKIEELREHLLKWGFTTPDKKHQKEPPFLWMGYELHPDKWTVQPIQLPEKD
SWTVNDIQKLVGKLNWASQIYPGIKVRQLCKLLRGAKALTDIVPLTEEAELELAENREILKEPVHGVYYD
PSKDLIAEIQKQGHDQWTYQIYQEPFKNLKTGKYAKMRTAHTNDVKQLTEAVQKIAMESIVIWGKTPKFR
LPIQKETWETWWTDYWQATWIPEWEFVNTPPLVKLWYQLEKEPIAGAETFYVDGAANRETKIGKAGYVTD
RGRQKIVSLTETTNQKTELQAIQLALQDSGSEVNIVTDSQYALGIIQAQPDKSESELVNQIIEQLIKKER
VYLSWVPAHKGIGGNEQVDKLVSSGIRKVLFLDGIDKAQEEHEKYHSNWRAMASEFNLPPIVAKEIVASC
DKCQLKGEAMHGQVDCSPGIWQLDCTHLEGKIILVAVHVASGYIEAEVIPAETGQETAYFILKLAGRWPV

KVIHTDNGSNFTSAAVKAACWWAGIQQEFGIPYNPQSQGVVESMNKELKKIIGQVRDQAEHLKTAVQMAV
FIHNFKRKGGIGGYSAGERIIDIIATDIQTKELQKQIIKIQNFRVYYRDSRDPIWKGPAKLLWKGEGAVV
IQDNSDIKVVPRRKAKIIKDYGKQMAGADCVAGRQDED

Figure 20A

B.con.gag (subtype B consensus gag. The amino acid sequence is different from Los Alamos Database August 2002)

GCCGCCGCCATGGGCGCCCGCGCCTCCGTGCTGTCCGGCGGCGAGCTGGA
CCGCTGGGAGAAGATCCGCCTGCGCCCCGGCGGCAAGAAGAAGTACAAGC
TGAAGCACATCGTGTGGGCCTCCCGCGAGCTGGAGCGCTTCGCCGTGAAC
CCCGGCCTGCTGGAGACCTCCGAGGGCTGCCGCCAGATCCTGGGCCAGCT
GCAGCCCTCCCTGCAGACCGGCTCCGAGGAGCTGCGCTCCCTGTACAACA
CCGTGGCCACCCTGTACTGCGTGCACCAGCGCATCGAGGTGAAGGACACC
AAGGAGGCCCTGGAGAAGATCGAGGAGGAGCAGAACAAGTCCAAGAAGAA
GGCCCAGCAGGCCGCCGCCGACACCGGCAACTCCTCCCAGGTGTCCCAGA
ACTACCCCATCGTGCAGAACCTGCAGGGCCAGATGGTGCACCAGGCCATC
TCCCCCCGCACCCTGAACGCCTGGGTGAAGGTGGTGGAGGAGAAGGCCTT
CTCCCCCGAGGTGATCCCCATGTTCTCCGCCCTGTCCGAGGGCGCCACCC
CCCAGGACCTGAACACCATGCTGAACACCGTGGGCGGCCACCAGGCCGCC
ATGCAGATGCTGAAGGAGACCATCAACGAGGAGGCCGCCGAGTGGGACCG
CCTGCACCCCGTGCACGCCGGCCCCATCGCCCCCGGCCAGATGCGCGAGC
CCCGCGGCTCCGACATCGCCGGCACCACCTCCACCCTGCAGGAGCAGATC
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ACCGCCTGCCAGGGCGTGGGCGGCCCCGGCCACAAGGCCCGCGTGCTGGC
CGAGGCCATGTCCCAGGTGACCAACTCCGCCACCATCATGATGCAGCGCG
GCAACTTCCGCAACCAGCGCAAGACCGTGAAGTGCTTCAACTGCGGCAAG
GAGGGCCACATCGCCAAGAACTGCCGCGCCCCCCGCAAGAAGGGCTGCTG
GAAGTGCGGCAAGGAGGGCCACCAGATGAAGGACTGCACCGAGCGCCAGG
CCAACTTCCTGGGCAAGATCTGGCCCTCCCACAAGGGCCGCCCCGGCAAC
TTCCTGCAGTCCCGCCCCGAGCCCACCGCCCCCCCCGAGGAGTCCTTCCG
CTTCGGCGAGGAGACCACCACCCCCTCCCAGAAGCAGGAGCCCATCGACA
AGGAGCTGTACCCCCTGGCCTCCCTGCGCTCCCTGTTCGGCAACGACCCC
TCCTCCCAGTAA

Figure 20B

B.con.env (subtype B consensus env. The amino acid sequence is different from Los Alamos Database August 2002)

GCCGCCGCCATGCGCGTGAAGGGCATCCGCAAGAACTACCAGCACCTGTG
GCGCTGGGGCACCATGCTGCTGGGCATGCTGATGATCTGCTCCGCCGCCG
AGAAGCTGTGGGTGACCGTGTACTACGGCGTGCCCGTGTGGAAGGAGGCC
ACCACCACCCTGTTCTGCGCCTCCGACGCCAAGGCCTACGACACCGAGGT
GCACAACGTGTGGGCCACCCACGCCTGCGTGCCCACCGACCCCAACCCCC
AGGAGGTGGTGCTGGAGAACGTGACCGAGAACTTCAACATGTGGAAGAAC
AACATGGTGGAGCAGATGCACGAGGACATCATCTCCCTGTGGGACCAGTC
CCTGAAGCCCTGCGTGAAGCTGACCCCCCTGTGCGTGACCCTGAACTGCA
CCGACCTGAAGAACAACCTGCTGAACACCAACTCCTCCTCCGGCGAGAAG
ATGGAGAAGGGCGAGATCAAGAACTGCTCCTTCAACATCACCACCTCCAT
CCGCGACAAGGTGCAGAAGGAGTACGCCCTGTTCTACAAGCTGGACGTGG
TGCCCATCGACAACAACAACAACACCTCCTACCGCCTGATCTCCTGCAAC
ACCTCCGTGATCACCCAGGCCTGCCCCAAGGTGTCCTTCGAGCCCATCCC
CATCCACTACTGCGCCCCCGCCGGCTTCGCCATCCTGAAGTGCAACGACA
AGAAGTTCAACGGCACCGGCCCCTGCACCAACGTGTCCACCGTGCAGTGC
ACCCACGGCATCCGCCCCGTGGTGTCCACCCAGCTGCTGCTGAACGGCTC
CCTGGCCGAGGAGGAGGTGGTGATCCGCTCCGAGAACTTCACCGACAACG
CCAAGACCATCATCGTGCAGCTGAACGAGTCCGTGGAGATCAACTGCACC
CGCCCCAACAACAACACCCGCAAGTCCATCCACATCGGCCCCGGCCGCGC
CTTCTACACCACCGGCGAGATCATCGGCGACATCCGCCAGGCCCACTGCA
ACATCTCCCGCGCCAAGTGGAACAACACCCTGAAGCAGATCGTGAAGAAG
CTGCGCGAGCAGTTCGGCAACAAGACCATCGTGTTCAACCAGTCCTCCGG
CGGCGACCCCGAGATCGTGATGCACTCCTTCAACTGCGGCGGCGAGTTCT
TCTACTGCAACACCACCCAGCTGTTCAACTCCACCTGGAACGACAACGGC
ACCTGGAACAACACCAAGGACAAGAACACCATCACCCTGCCCTGCCGCAT
CAAGCAGATCATCAACATGTGGCAGGAGGTGGGCAAGGCCATGTACGCCC
CCCCCATCCGCGGCCAGATCCGCTGCTCCTCCAACATCACCGGCCTGCTG
CTGACCCGCGACGGCGGCAACAACAACAACGACACCGAGATCTTCCGCCC
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AACCTGCTGCGCGCCATCGAGGCCCAGCAGCACCTGCTGCAGCTGACCGT
GTGGGGCATCAAGCAGCTGCAGGCCCGCGTGCTGGCCGTGGAGCGCTACC
TGAAGGACCAGCAGCTGCTGGGCATCTGGGGCTGCTCCGGCAAGCTGATC
TGCACCACCACCGTGCCCTGGAACGCCTCCTGGTCCAACAAGTCCCTGGA
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GAGAAGAACGAGCAGGAGCTGCTGGAGCTGGACAAGTGGGCCTCCCTGTG
GAACTGGTTCGACATCACCAACTGGCTGTGGTACATCAAGATCTTCATCA
TGATCGTGGGCGGCCTGATCGGCCTGCGCATCGTGTTCGCCGTGCTGTCC
ATCGTGAACCGCGTGCGCCAGGGCTACTCCCCCCTGTCCTTCCAGACCCG
CCTGCCCGCCCCCCGCGGCCCCGACCGCCCCGAGGGCATCGAGGAGGAGG
GCGGCGAGCGCGACCGCGACCGCTCCGGCCGCCTGGTGGACGGCTTCCTG
GCCCTGATCTGGGACGACCTGCGCTCCCTGTGCCTGTTCTCCTACCACCG
CCTGCGCGACCTGCTGCTGATCGTGACCCGCATCGTGGAGCTGCTGGGCC
GCCGCGGCTGGGAGGTGCTGAAGTACTGGTGGAACCTGCTGCAGTACTGG
TCCCAGGAGCTGAAGAACTCCGCCGTGTCCCTGCTGAACGCCACCGCCAT
CGCCGTGGCCGAGGGCACCGACCGCGTGATCGAGGTGGTGCAGCGCGCCT
GCCGCGCCATCCTGCACATCCCCCGCCGCATCCGCCAGGGCCTGGAGCGC
GCCCTGCTGTAA

Figure 20C

B.con.gag (subtype B consensus gag)
MGARASVLSGGELDRWEKIRLRPGGKKKYKLKHIVWASRELERFAVNPGLLETSEGCRQILGQLQPSLQT
GSEELRSLYNTVATLYCVHQRIEVKDTKEALEKIEEEQNKSKKKAQQAAADTGNSSQVSQNYPIVQNLQG
QMVHQAISPRTLNAWVKVVEEKAFSPEVIPMFSALSEGATPQDLNTMLNTVGGHQAAMQMLKETINEEAA
EWDRLHPVHAGPIAPGQMREPRGSDIAGTTSTLQEQIGWMTNNPPIPVGEIYKRWIILGLNKIVRMYSPT
SILDIRQGPKEPFRDYVDRFYKTLRAEQASQEVKNWMTETLLVQNANPDCKTILKALGPAATLEEMMTAC
QGVGGPGHKARVLAEAMSQVTNSATIMMQRGNFRNQRKTVKCFNCGKEGHIAKNCRAPRKKGCWKCGKEG
HQMKDCTERQANFLGKIWPSHKGRPGNFLQSRPEPTAPPEESFRFGEETTTPSQKQEPIDKELYPLASLR
SLFGNDPSSQ

B.con.env (subtype B consensus env)
MRVKGIRKNYQHLWRWGTMLLGMLMICSAAEKLWVTVYYGVPVWKEATTTLFCASDAKAYDTEVHNVWAT
HACVPTDPNPQEVVLENVTENFNMWKNNMVEQMHEDIISLWDQSLKPCVKLTPLCVTLNCTDLKNNLLNT
NSSSGEKMEKGEIKNCSFNITTSIRDKVQKEYALFYKLDVVPIDNNNNTSYRLISCNTSVITQACPKVSF
EPIPIHYCAPAGFAILKCNDKKFNGTGPCTNVSTVQCTHGIRPVVSTQLLLNGSLAEEEVVIRSENFTDN
AKTIIVQLNESVEINCTRPNNNTRKSIHIGPGRAFYTTGEIIGDIRQAHCNISRAKWNNTLKQIVKKLRE
QFGNKTIVFNQSSGGDPEIVMHSFNCGGEFFYCNTTQLFNSTWNDNGTWNNTKDKNTITLPCRIKQIINM
WQEVGKAMYAPPIRGQIRCSSNITGLLLTRDGGNNNNDTEIFRPGGGDMRDNWRSELYKYKVVKIEPLGV
APTKAKRRVVQREKRAVGIGAMFLGFLGAAGSTMGAASMTLTVQARQLLSGIVQQQNNLLRAIEAQQHLL
QLTVWGIKQLQARVLAVERYLKDQQLLGIWGCSGKLICTTTVPWNASWSNKSLDEIWDNMTWMEWEREID
NYTSLIYTLIEESQNQQEKNEQELLELDKWASLWNWFDITNWLWYIKIFIMIVGGLIGLRIVFAVLSIVN
RVRQGYSPLSFQTRLPAPRGPDRPEGIEEEGGERDRDRSGRLVDGFLALIWDDLRSLCLFSYHRLRDLLL
IVTRIVELLGRRGWEVLKYWWNLLQYWSQELKNSAVSLLNATAIAVAEGTDRVIEVVQRACRAILHIPRR
IRQGLERALL

Figure 20D

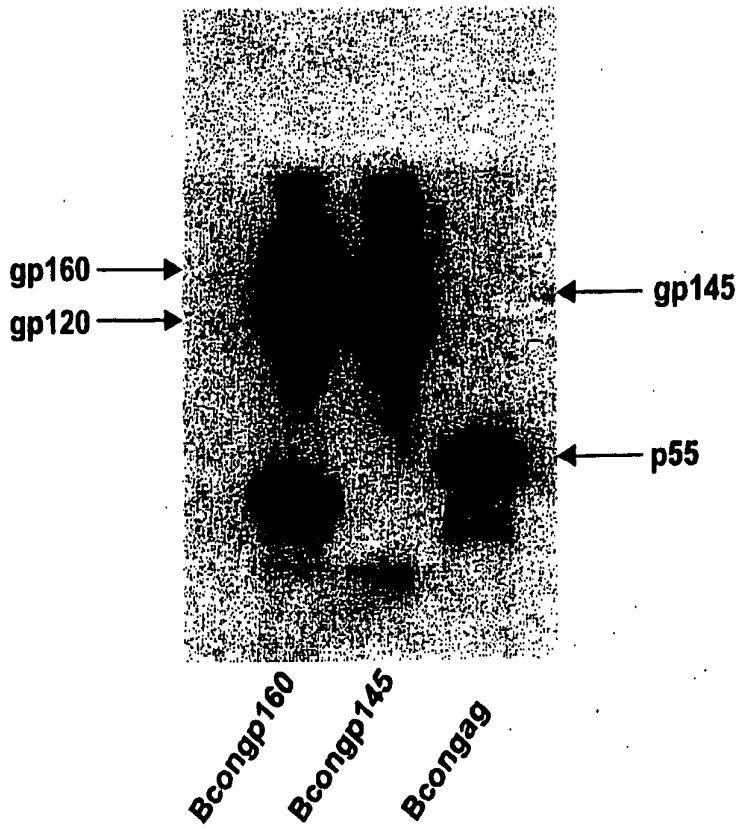
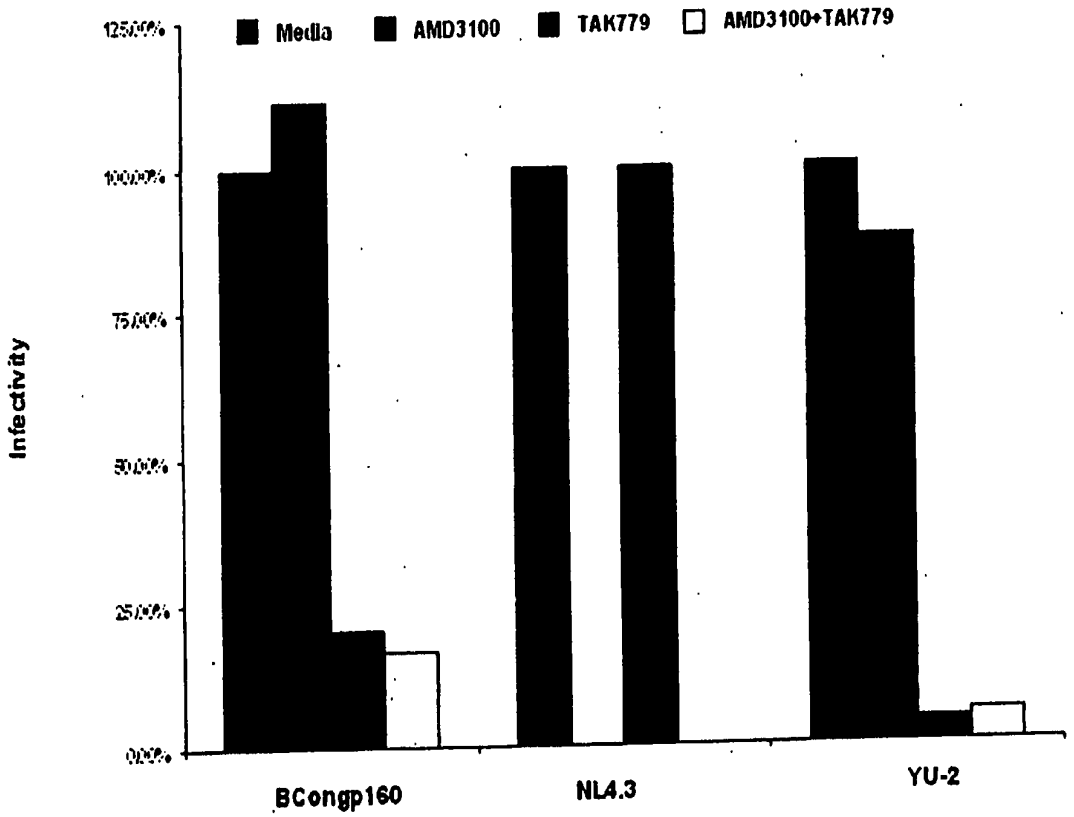


Figure 21. Expression of subtype B consensus *env* and *gag* genes in 293T cells. Plasmids containing codon-optimized subtype B consensus *gp160, gp140*, and *gag* genes were transfected into 293T cells, and protein expression was examined by Western Blot analysis of cell lysates. 48-hours post-transfection, cell lysates were collected, total protein content determined by the BCA protein assay, and 2 μg of total protein was loaded per lane on a 4-20% SDS-PAGE gel. Proteins were transferred to a PVDF membrane and probed with serum from an HIV-1 subtype B infected individual.

Figure 22



Co-receptor usage of subtype B consensus envelopes. Pseudotyped particles containing the subtype B consensus gp160 Env were incubated with DEAE-Dextran treated JC53-BL cells in the presence of AMD3100 (a specific inhibitor of CXCR4), TAK779 (a specific inhibitor of CCR5), and AMD3000+TAK779 to determine co-receptor usage. NL4.3, an isolate known to utilize CXCR4 and YU-2, a known CCR5-using isolate, were included as controls.

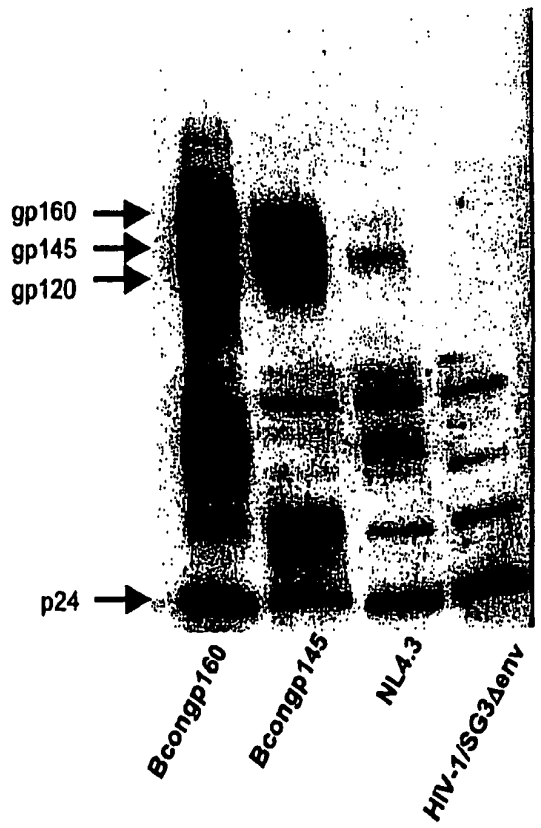


Figure 23A. ***Trans* complementation of *env*-deficient HIV-1 with codon-optimized subtype B consensus *gp160* and *gp140* genes.**

Plasmids containing codon-optimized, subtype B consensus *gp160* or *gp140* genes were co-transfected into 293T cells with an HIV-1/SG3Δenv provirus. 48-hours post-transfection cell supernatants containing pseudotyped virus were harvested, clarified in a tabletop centrifuge, filtered through a 0.2μM filter, and pellet through a 20% sucrose cushion. Quantification of p24 in each virus pellet was determined using the Coulter HIV-1 p24 antigen assay; 25 ng of p24 was loaded per lane on a 4-20% SDS-PAGE gel. Proteins were transferred to a PVDF membrane and probed with anti-HIV-1 antibodies from infected HIV-1 subtype B patient serum. *Trans* complementation with a rev-dependent NL4.3 *env* was included for control.

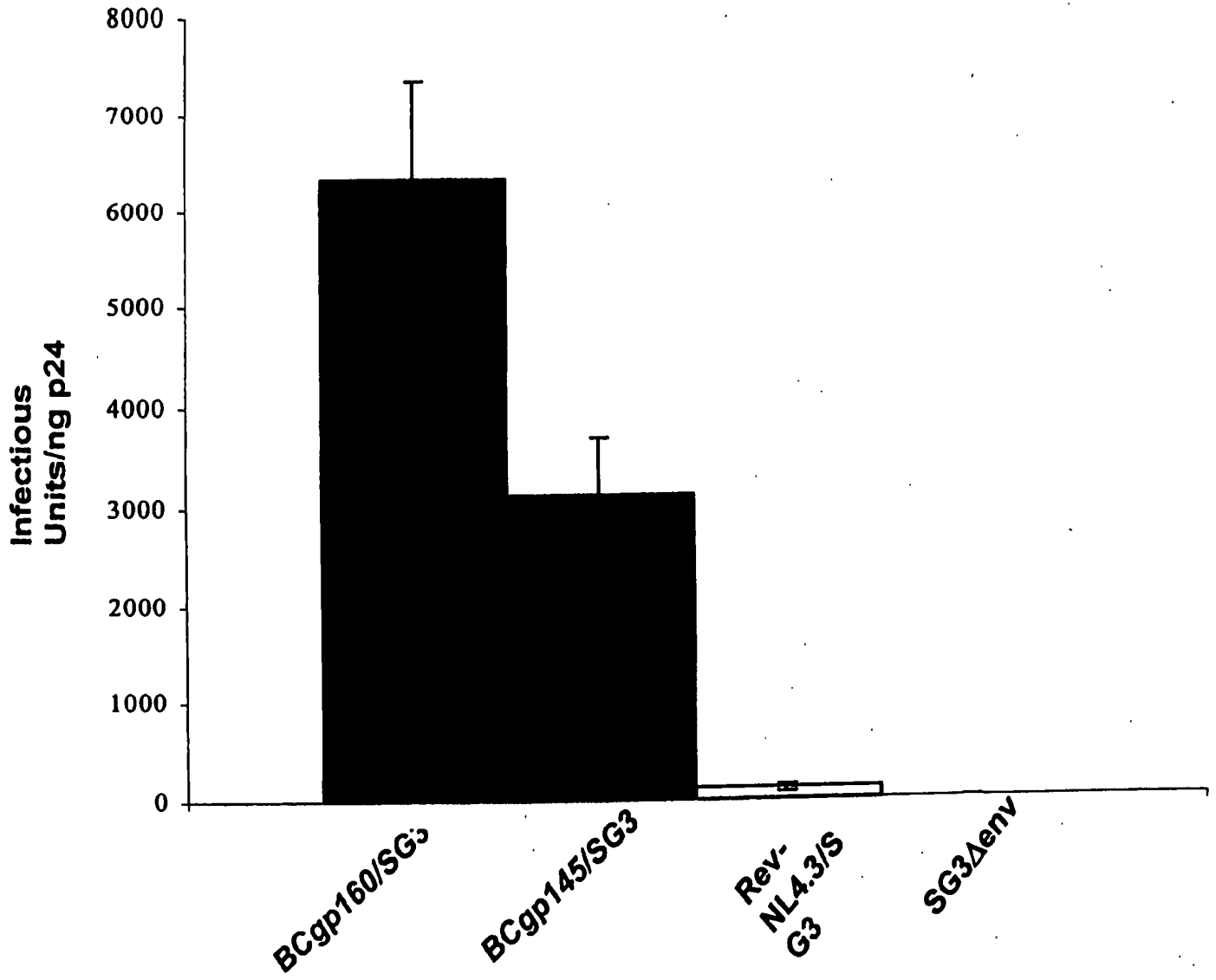
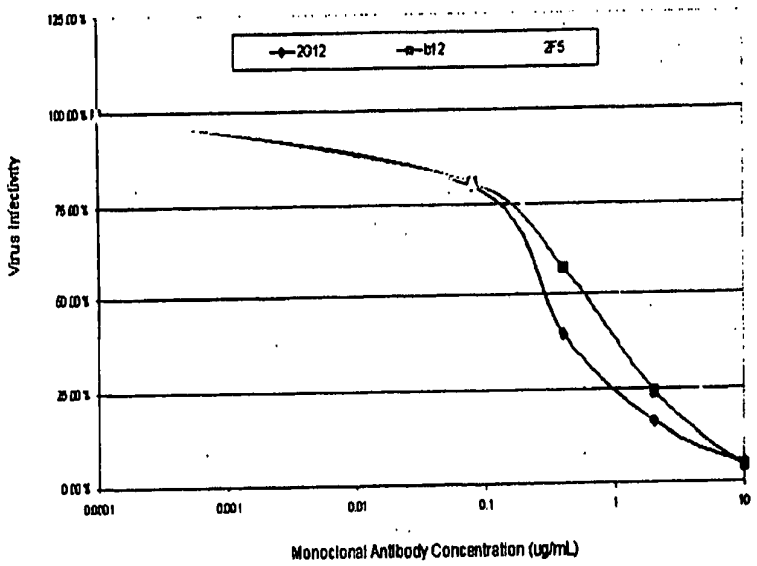


Figure 238 **Infectivity of virus particles containing the subtype B concensus envelope.**

Infectivity of pseudotyped virus containing consensus B gp160 or gp140 was determined using the JC53-BL assay. Sucrose cushion purified virus particles were assayed by the Coulter p24 antigen assay, and 5-fold serial dilutions of each pellet were incubated with DEAE-Dextran treated JC53-BL cells. Following a 48-hour incubation period, cells were fixed and stained to visualize β-galactosidase expressing cells. Infectivity is expressed as infectious units per ng of p24.

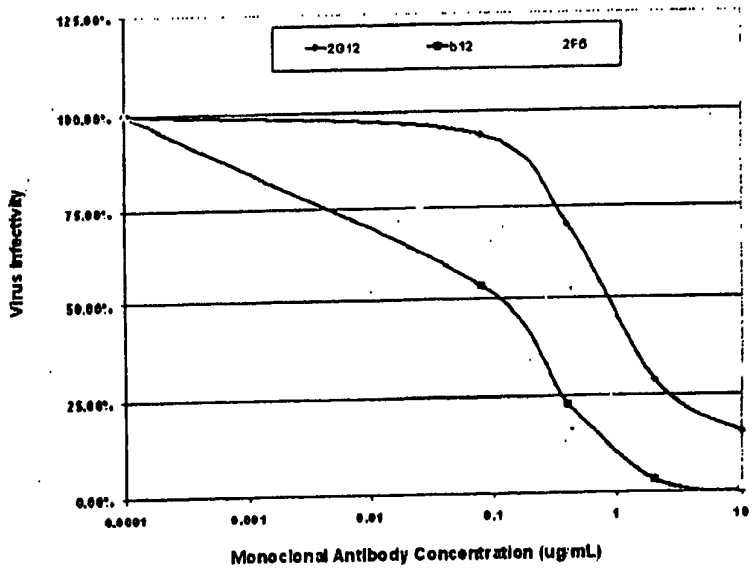
Figure 24

A



Neutralization of Pseudovirions containing Subtype B consensus Env (gp160)

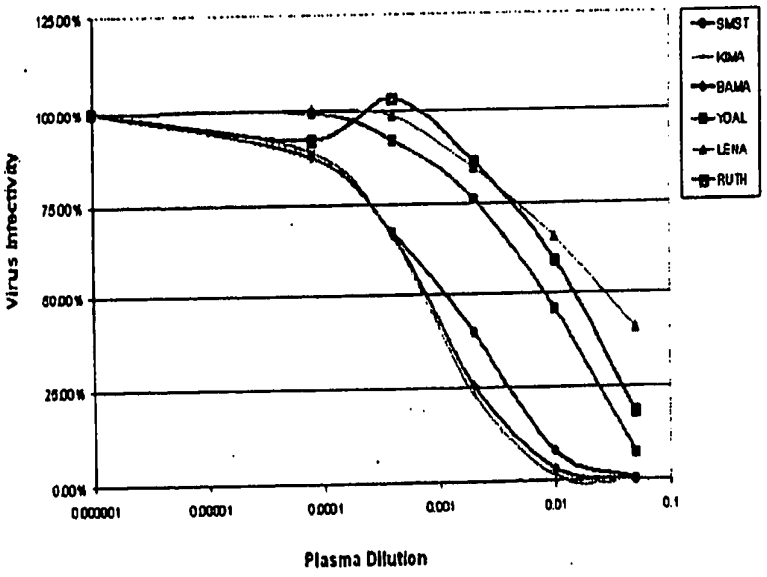
B



Neutralization of Pseudovirions containing NL4.3 Env (gp160)

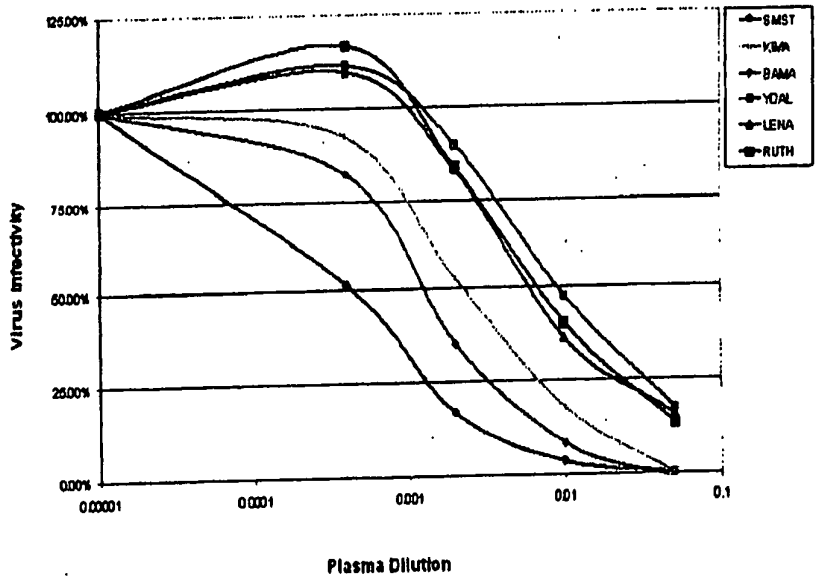
FIGURE 24

C



Neutralization of Pseudovirions containing Subtype B consensus Env (gp160)

D

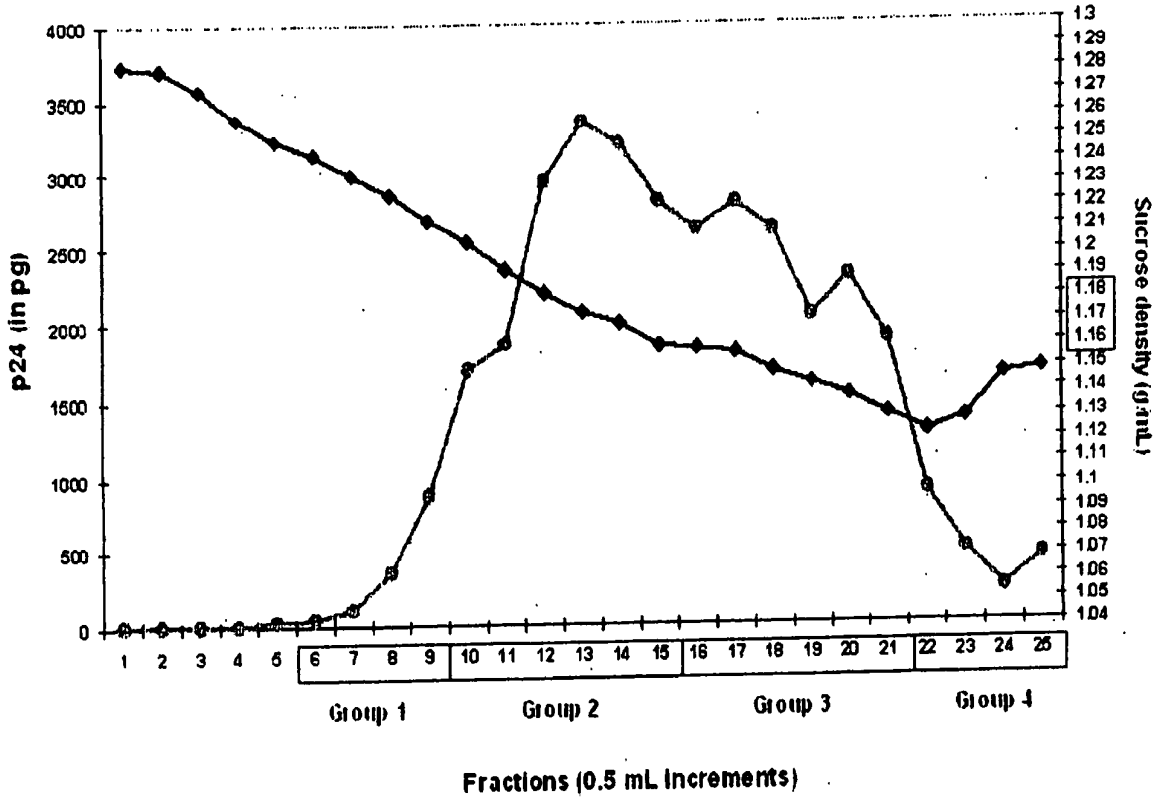


Neutralization of Pseudovirions containing NL4.3 Env (gp160)

Neutralization sensitivity of virions containing subtype B concensus gp 160 envelope.

Equivalent amounts of pseudovirions containing the subtype B consensus or NL4.3 Env (gp160) (1,500 infectious units) were preincubated with three different monoclonal neutralizing antibodies and a panel of plasma samples from HIV-1 subtype B infected individuals, and then added to the JC53-BL cell monolayer in 96-well plates. Plates were cultured for two days and luciferase activity was measured as an indicator of viral infectivity. Virus infectivity was calculated by dividing the luciferase units (LU) produced at each concentration of antibody by the LU produced by the control infection. The mean 50% inhibitory concentration (IC_{50}) and the actual % neutralization at each antibody dilution were then calculated for each virus. The results of all luciferase experiments were confirmed by direct counting of blue foci in parallel infections.

Figure 25 A



Density and p24 analysis of sucrose gradient fractions.

0.5ml fractions were collected from a 20-60% sucrose gradient. Fraction number 1 represents the most dense fraction taken from the bottom of the gradient tube. Density was measured with a refractometer and the amount of p24 in each fraction was determined by the Coulter p24 antigen assay. Fractions 6-9, 10-15, 16-21, and 22-25 were pooled together and analyzed by Western Blot. As expected, virions sedimented at a density of 1.16-1.18 g/ml.

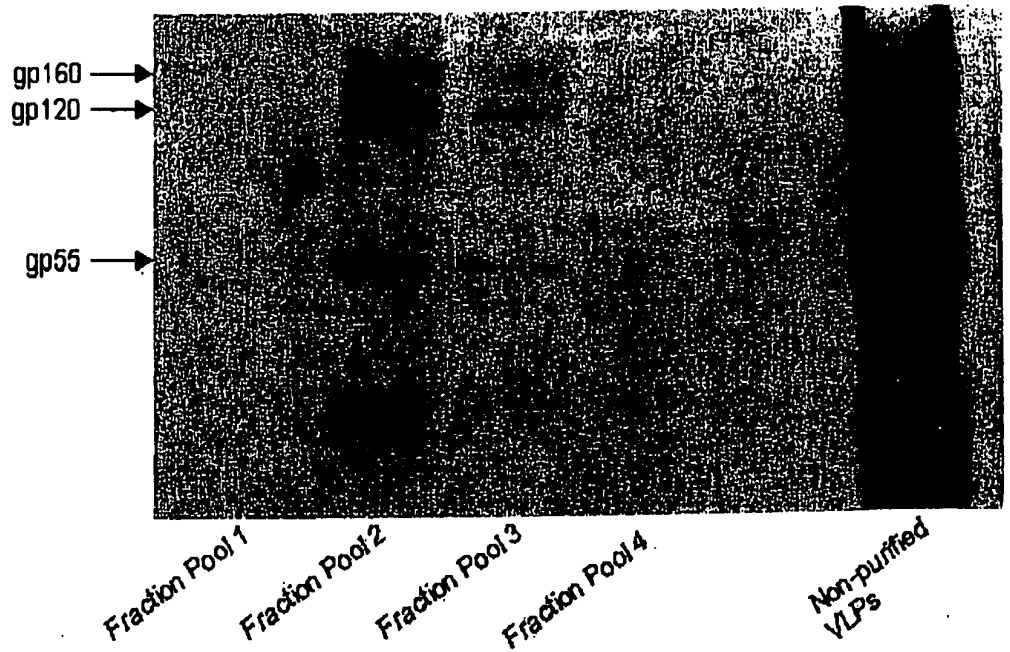


Figure 25B **VLP production by co-transfection of subtype B consensus *gag* and *env* genes.**

293T cells were co-transfected with subtype B consensus *gag* and *env* genes. Cell supernatants were harvested 48-hours post-transfection, clarified through at 20% sucrose cushion, and further purified through a 20-60% sucrose gradient. Select fractions from the gradient were pooled, added to 20ml of PBS, and centrifuged overnight at 100,000 x g. Resuspended pellets were loaded onto a 4-20% SDS-PAGE gel, proteins were transferred to a PVDF membrane, and probed with plasma from an HIV-1 subtype B infected individual.

Figure 26

A

Year 2000 Con-S 140CFI.Env

MRVRGIQRNCQHLWRWGTLILGMLMICSAAENLWVTVYYGVPVWKEANTTLFCASDAKAYDTEVH
NVWATHACVPTDPNPQEIVLENVTENFNMWKNNMVEQMHEDIISLWDQSLKPCVKLTPLCVTLNC
TNVNVTNTTNNTEEKGEIKNCSFNITTEIRDKKQKVYALFYRLDVVPIDDNNNNSSNYRLINCNT
SAITQACPKVSFEPIPIHYCAPAGFAILKCNDKKFNGTGPCKNVSTVQCTHGIKPVVSTQLLLNG
SLAEEEIIIRSENITNNAKTIIVQLNESVEINCTRPNNNTRKSIRIGPGQAFYATGDIIGDIRQA
HCNISGTKWNKTLQQVAKKLREHFNNKTIIFKPSSGGDLEITTHSFNCRGEFFYCNTSGLFNSTW
IGNGTKNNNNTNDTITLPCRIKQIINMWQGVGQAMYAPPIEGKITCKSNITGLLLTRDGGNNNTN
ETEIFRPGGGDMRDNWRSELYKYKVVKIEPLGVAPTKAKLTVQARQLLSGIVQQQSNLLRAIEAQ
QHLLQLTVWGIKQLQARVLAVERYLKDQQLEIWDNMTWMEWEREINNYTDIIYSLIEESQNQQEK
NEQELLALDKWASLWNWFDITNWLW

A gp140 CFI is referred to HIV-1 envelope design with the cleavage-site-deleted (C), fusion-site-deleted (F) and gp41 immunodominant region-deleted (I) in addition to the deletion of transmembrane and cytoplasmic domains.

Codon-optimized Year 2000 Con-S 140CFI. seq

B

ATGCGCGTGCGCGGCATCCAGCGCAACTGCCAGCACCTGTGGCGCTGGGGCACCCTGATCCTGGG
CATGCTGATGATCTGCTCCGCCGCCGAGAACCTGTGGGTGACCGTGTACTACGGCGTGCCCGTGT
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AACGTGTGGGCCACCCACGCCTGCGTGCCCACCGACCCCAACCCCCAGGAGATCGTGCTGGAGAA
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CCCTGTGGGACCAGTCCCTGAAGCCCTGCGTGAAGCTGACCCCCCTGTGCGTGACCCTGAACTGC
ACCAACGTGAACGTGACCAACACCACCAACAACACCGAGGAGAAGGGCGAGATCAAGAACTGCTC
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TCCGCATCGGCCCCGGCCAGGCCTTCTACGCCACCGGCGACATCATCGGCGACATCCGCCAGGCC
CACTGCAACATCTCCGGCACCAAGTGGAACAAGACCCTGCAGCAGGTGGCCAAGAAGCTGCGCGA
GCACTTCAACAACAAGACCATCATCTTCAAGCCCTCCTCCGGCGGCGACCTGGAGATCACCACCC
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AGATCAACAACTACACCGACATCATCTACTCCCTGATCGAGGAGTCCCAGAACCAGCAGGAGAAG
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Figure 27

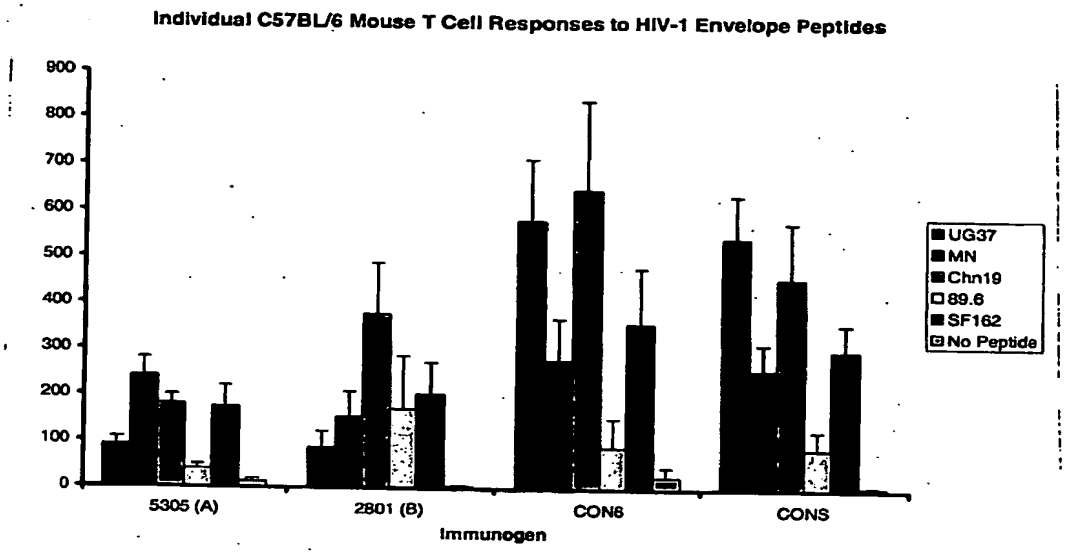
Individual C57BL/6 Mouse T Cell Responses to HIV-1 Envelope Peptides
900
800
700
600
500
400
300
200
100
0
5305 (A)
2801 (B)
CON6
CONS
Immunogen
UG37
MN
Chn19
89.6
SF162
No Peptide

Fig. 28

Design of expression-optimized HIV-1 envelope gp140CF

A

Con-B-2003 Env.pep (841 a.a.)*

MRVKGIRKNYQHLWRWGTMLLGMLMICSAAEKLWVTVYYGVPVWKEATTTLFCASDAKAYDTEVHNVWATHACVPTDPNPQEVVL
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ALFYKLDVVPIDNDNTSYRLISCNTSVITQACPKVSFEPIPIHYCAPAGFAILKCNDKKFNGTGPCTNVSTVQCTHGIRPVVSTQ
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IVKKLREQFGNKTIVFNQSSGGDPEIVMHSFNCGGEFFYCNTTQLFNSTWNGTWNNTEGNITLPCRIKQIINMWQEVGKAMYAPP
IRGQIRCSSNITGLLLTRDGGNNETEIFRPGGGDMRDNWRSELYKYKVVKIEPLGVAPTKAKRRVVQREKRAVGIGAMFLGFLGA
AGSTMGAASMTLTVQARQLLSGIVQQQNNLLRAIEAQQHLLQLTVWGIKQLQARVLAVERYLKDQQLLGIWGCSGKLICTTAVPW
NASWSNKSLDEIWDNMTWMEWEREIDNYTSLIYTLIEESQNQQEKNEQELLELDKWASLWNWFDITNWLWYIKIFIMIVGGLVGL
RIVFAVLSIVNRVRQGYSPLSFQTRLPAPRGPDRPEGIEEEGGERDRDRSGRLVDGFLALIWDDLRSLCLFSYHRLRDLLLIVTR
IVELLGRRGWEVLKYWWNLLQYWSQELKNSAVSLLNATAIAVAEGTDRVIEVVQRACRAILHIPRRIRQGLERALL

*Amino acid sequence underlined is the fusion domain that will be deleted in 140CF design and the "W" underlined with red color is the last amino acid at the C terminus, and all the remaining amino acids after the "W" will be deleted in 140CF design.

3

Con-B-140CF.pep (632 a.a.)
Nick name: 002

MRVKGIRKNYQHLWRWGTMLLGMLMICSAAEKLWVTVYYGVPVWKEATTTLFCASDAKAYDTEVHNVWATHACVPTDPNPQEVVL
ENVTENFNMWKNNMVEQMHEDIISLWDQSLKPCVKLTPLCVTLNCTDLMNATNTNTTIIYRWRGEIKNCSFNITTSIRDKVQKEY
ALFYKLDVVPIDNDNTSYRLISCNTSVITQACPKVSFEPIPIHYCAPAGFAILKCNDKKFNGTGPCTNVSTVQCTHGIRPVVSTQ
LLLNGSLAEEEVVIRSENFTDNAKTIIVQLNESVEINCTRPNNNTRKSIHIGPGRAFYTTGEIIGDIRQAHCNISRAKWNNTLKQ
IVKKLREQFGNKTIVFNQSSGGDPEIVMHSFNCGGEFFYCNTTQLFNSTWNGTWNNTEGNITLPCRIKQIINMWQEVGKAMYAPP
IRGQIRCSSNITGLLLTRDGGNNETEIFRPGGGDMRDNWRSELYKYKVVKIEPLGVAPTKAK**TLTVQARQLLSGIVQQQNNLLRA**
IEAQQHLLQLTVWGIKQLQARVLAVERYLKDQQLLGIWGCSGKLICTTAVPWNASWSNKSLDEIWDNMTWMEWEREIDNYTSLIY
TLIEESQNQQEKNEQELLELDKWASLWNWFDITNWLW*

*Amino acids seen in blue color is for easy identification of the junction of the deleted fusion cleavage site.

3

Codon-opitmized Con-B 140CF.seq (1927 nt.)
Nick name: 002

TTCAGTCGACGGCCACCATGAGGGTGAAGGGTATTCGGAAAAATTACCAACACCTGTGGCGCTGGGGAACCATGCTCCTTGGTAT
GCTGATGATTTGCAGTGCCGCCGAGAAACTTTGGGTAACTGTGTACTACGGCGTTCCTGTCTGGAAGGAAGCTACAACCACTCTT
TTTTGTGCATCCGACGCTAAAGCTTACGACACAGAAGTGCATAATGTTTGGGCCACCCATGCTTGCGTCCCTACAGATCCCAACC
CCCAGGAAGTCGTCCTTGAGAATGTCACAGAGAATTTTAACATGTGGAAGAATAATATGGTAGAACAAATGCACGAAGACATTAT
TAGCCTGTGGGACCAGTCCTTGAAGCCCTGCGTGAAACTCACTCCACTTTGCGTCACACTTAACTGTACTGATTTGATGAACGCA
ACCAACACAAATACTACTATTATATATCGCTGGAGGGGGGAAATCAAGAACTGCTCTTTCAACATCACCACTTCCATAAGGGATA
AGGTCCAGAAAGAATATGCCCTGTTTTATAAACTTGATGTGGTCCCGATAGACAATGACAACACTAGCTATCGACTGATCTCTTG
TAACACATCCGTGATTACCCAAGCTTGCCCAAAGGTCAGCTTTGAACCAATACCCATTCACTACTGCGCTCCCGCTGGTTTTGCC
ATCCTCAAGTGTAACGACAAAAAATTCAATGGGACCGGACCTTGCACAAACGTGTCCACCGTGCAATGTACTCACGGAATCAGAC
CTGTTGTCAGTACCCAACTCCTCTTGAACGGGTCTCTCGCGGAAGAGGAGGTCGTGATTAGAAGCGAAAACTTTACCGATAACGC
TAAAACAATCATTGTGCAACTTAATGAAAGCGTCGAAATTAACTGCACCAGACCAAACAATAATACCAGAAAATCTATTCACATA
GGGCCCGGCCGCGCATTTTATACAACTGGCGAAATCATTGGTGACATCAGACAAGCTCATTGCAATATCTCCCGCGCGAAATGGA
ACAACACCCTGAAACAGATCGTGAAGAAACTTCGAGAACAATTCGGTAATAAAACAATCGTATTCAACCAAAGCTCCGGAGGCGA
CCCTGAGATAGTTATGCACTCATTCAACTGTGGCGGCGAGTTCTTCTATTGTAACACAACTCAACTTTTTAATAGCACTTGGAAT
GGAACATGGAACAACACAGAAGGGAACATCACTCTGCCTTGTCGGATTAAGCAGATCATTAATATGTGGCAAGAAGTGGGAAAAG
CTATGTACGCCCCGCCTATTCGCGGACAAATAAGATGCTCTAGTAATATTACCGGATTGTTGCTGACACGCGACGGAGGAAATAA
TGAAACAGAGATATTTAGACCTGGCGGAGGCGACATGAGAGATAACTGGAGAAGTGAGCTTTACAAATATAAAGTCGTAAAGATA
GAACCATTGGGGGTAGCACCAACCAAAGCAAAAACCTTGACAGTACAGGCTAGGCAGCTGCTGAGCGGAATCGTGCAACAACAAA
ATAATCTTCTCCGAGCCATAGAAGCACAACAACATCTGTTGCAGCTGACAGTATGGGGAATCAAACAGCTTCAGGCAAGAGTGCT
GGCCGTCGAGAGATACCTCAAAGATCAACAACTGCTGGGCATATGGGGATGTTCCGGTAAACTCATATGCACTACCGCCGTGCCC
TGGAACGCGAGCTGGTCTAATAAATCCCTGGATGAAATTTGGGACAACATGACTTGGATGGAATGGGAACGGGAAATTGACAACT
ATACTAGTTTGATTTATACTCTGATCGAAGAATCTCAGAACCAACAGGAGAAAAACGAACAGGAACTGCTGGAACTGGACAAGTG
GGCATCATTGTGGAACTGGTTTGACATTACTAACTGGCTGTGGTAAAGATCTTACAA

(For all 140CF design shown here and below, 140CF gene will be flanked with the 5' sequence of "TTCAGTCGACGGCCACC" that contains a Kozak" sequence (GCCACCATGG/A) and *SalI* site and 3'sequence of TAAAGATCTTACAA containing stop codon and *BglII* site.)

Fig. 29

4

CON_OF_CON-S-2003 (829 a.a.)

MRVMGIQRNCQHLWRWGILIFGMLIICSAAENLWVTVYYGVPVWKEANTTLFCASDAKAYDTEVHNVWATHACVPTDPNPQEIVL
ENVTENFNMWKNNMVEQMHEDIISLWDQSLKPCVKLTPLCVTLNCTDVNATNNTTNNEEIKNCSFNITTEIRDKKKKVYALFYKL
DVVPIDDNNSYRLINCNTSAITQACPKVSFEPIPIHYCAPAGFAILKCNDKKFNGTGPCKNVSTVQCTHGIKPVVSTQLLLNGSL
AEEEIIIRSENITNNAKTIIVQLNESVEINCTRPNNNTRKSIRIGPGQAFYATGDIIGDIRQAHCNISRTKWNKTLQQVAKKLRE

HFNKTIIFNPSSGGDLEITTHSFNCGGEFFYCNTSELFNSTWNGTNNTITLPCRIKQIINMWQGVGQAMYAPPIEGKIRCTSNIT
GLLLTRDGGNNNTETFRPGGGDMRDNWRSELYKYKVVKIEPLGVAPTKAKRRVVEREKRAVGIGAVFLGFLGAAGSTMGAASITL
TVQARQLLSGIVQQQSNLLRAIEAQQHLLQLTVWGIKQLQARVLAVERYLKDQQLLGIWGCSGKLICTTNVPWNSSWSNKSQDEI
WDNMTWMEWDKEINNYTDIIYSLIEESQNQQEKNEQELLALDKWASLWNWFDITNWLWYIKIFIMIVGGLIGLRIVFAVLSIVNR
VRQGYSPLSFQTLIPNPRGPDRPEGIEEEGGEQDRDRSIRLVNGFLALAWDDLRSLCLFSYHRLRDLILIAARTVELLGRRGWEA
LKYLWNLLQYWGQELKNSAISLLDTTAIAVAEGTDRVIEVVQRVCRAILNIPRRIRQGFERALL
*Amino acid sequence underlined is the fusion domain that will be deleted in 140CF design and the "W" underlined with red color is the last amino acid at the C terminus, and all the remaining amino acids after the "W" will be deleted in 140CF design.

B

CON-S-2003 140CF.pep (620 a.a.).
Nick name: 006
MRVMGIQRNCQHLWRWGILILFGMLIICSAAENLWVTVYYGVPVWKEANTTLFCASDAKAYDTEVHNVWATHACVPTDPNPQEIVL
ENVTENFNMWKNNMVEQMHEDIISLWDQSLKPCVKLTPLCVTLNCTDVNATNNTTNNEEIKNCSFNITTEIRDKKKKVYALFYKL
DVVPIDDNNSYRLINCNTSAITQACPKVSFEPIPIHYCAPAGFAILKCNDKKFNGTGPCKNVSTVQCTHGIKPVVSTQLLLNGSL
AEEEIIIRSENITNNAKTIIVQLNESVEINCTRPNNNTRKSIRIGPGQAFYATGDIIGDIRQAHCNISRTKWNKTLQQVAKKLRE
HFNKTIIFNPSSGGDLEITTHSFNCGGEFFYCNTSELFNSTWNGTNNTITLPCRIKQIINMWQGVGQAMYAPPIEGKIRCTSNIT
GLLLTRDGGNNNTETFRPGGGDMRDNWRSELYKYKVVKIEPLGVAPTKAK**TLTVQARQLLSGIVQQQSNLLRAIEAQQHLLQLTV**
WGIKQLQARVLAVERYLKDQQLLGIWGCSGKLICTTNVPWNSSWSNKSQDEIWDNMTWMEWDKEINNYTDIIYSLIEESQNQQEK
NEQELLALDKWASLWNWFDITNWLW*
*Amino acids seen in blue color is for easy identification of the junction of the deleted fusion cleavage site.

C

CODON-OPTIMIZED CON-S-2003 140CF.seq (1891 nt.)
Nick name :006
TTCAGTCGACAGCCACCATGCGGGTCATGGGGATACAGAGGAATTGCCAGCACTTGTGGAGGTGGGGAATTTTGATATTCGGGAT
GCTCATAATCTGCTCTGCCGCTGAGAACCTGTGGGTCACTGTGTATTACGGCGTTCCCGTCTGGAAAGAAGCTAATACTACCCTG
TTTTGTGCAAGCGACGCCAAAGCATACGACACCGAAGTCCACAATGTCTGGGCTACCCACGCCTGTGTACCTACTGATCCAAATC
CCCAGGAAATTGTTCTTGAAAACGTAACGGAAAACTTTAACATGTGGAAGAATAATATGGTGGAGCAAATGCACGAGGATATAAT
CAGCCTGTGGGACCAGTCCCTCAAACCATGCGTTAAACTCACTCCACTCTGCGTGACTCTGAACTGTACCGACGTGAACGCAACC
AATAATACAACAAACAATGAGGAGATAAAGAATTGTTCATTTAATATAACCACTGAGATACGGGATAAGAAAAAAAAGGTTTATG
CACTCTTTTACAAGCTCGACGTGGTGCCCATAGACGACAATAATAGCTACCGACTCATTAATTGCAATACTAGCGCTATAACCCA
GGCATGCCCCAAAGTTTCCTTCGAGCCCATACCGATTCACTACTGCGCACCCGCCGGATTCGCCATTCTTAAATGCAATGACAAG
AAGTTCAACGGCACCGGACCCTGTAAGAACGTAAGCACTGTTCAATGTACACATGGAATTAAGCCGGTAGTGTCAACGCAGCTCC
TCCTCAACGGAAGCCTTGCAGAAGAAGAGATCATTATCAGGTCAGAAAATATCACTAACAACGCGAAAACAATCATTGTTCAGCT
GAATGAGTCTGTAGAAATCAATTGTACCCGCCCTAATAATAACACAAGAAAGTCAATTAGGATCGGACCCGGCCAGGCTTTCTAC
GCAACCGGAGATATCATCGGGGATATACGACAGGCCCACTGCAACATTTCTAGAACTAAGTGGAATAAAACTTTGCAGCAGGTAG
CCAAGAAACTGCGGGAACATTTTAATAAGACAATCATCTTCAATCCAAGTAGCGGAGGGGACCTGGAAATCACTACACATTCCTT
TAACTGTGGGGGCGAGTTTTTCTACTGTAATACCTCTGAACTGTTCAACTCAACATGGAATGGCACTAACAATACTATAACTCTT
CCTTGCAGAATAAAACAGATTATCAACATGTGGCAGGGTGTGGGGCAAGCAATGTATGCACCACCAATCGAAGGCAAAATAAGAT
GCACCTCCAATATTACCGGACTCCTCCTGACACGGGATGGCGGAAACAATAACACGGAGACCTTTAGGCCAGGCGGCGGCGATAT
GAGAGATAACTGGCGCTCCGAGCTCTATAAATACAAAGTCGTTAAGATCGAGCCCCTTGGAGTTGCGCCAACCAAAGCTAAAACC
TTGACCGTGCAAGCCAGGCAGTTGTTGTCAGGTATCGTACAGCAGCAATCTAATCTTTTGAGAGCCATTGAGGCTCAGCAGCACC
TCTTGCAGCTTACCGTCTGGGGCATCAAACAACTTCAGGCACGCGTCCTGGCCGTAGAGCGCTATTTGAAAGACCAACAACTTCT
CGGGATCTGGGGGTGTTCTGGAAAATTGATCTGCACGACAAATGTGCCTTGGAACAGCAGCTGGTCAAATAAAAGCCAAGACGAA
ATATGGGATAACATGACATGGATGGAATGGGATAAAGAAATTAATAATTACACTGACATTATTTACTCACTTATCGAGGAATCAC
AAAATCAACAGGAAAAAAATGAACAGGAACTCTTGGCTCTGGACAAATGGGCTTCACTGTGGAACTGGTTCGACATCACAAATTG
GCTCTGGTAAAGATCTTACAA

Fig.30

A

CONSENSUS_A1-2003(845 a.a.)
MRVMGIQRNCQHLLRWGTMILGMIIICSAAENLWVTVYYGVPVWKDAETTLFCASDAKAYETEMHNVWATHACVPTDPNPQEIHL
ENVTEEFNMWKNNMVEQMHTDIISLWDQSLKPCVKLTPLCVTLNCSNVNVTNNTTNTHEEEIKNCSFNMTTELRDKKQKVYSLFY
RLDVVQINENNSNSSYRLINCNTSAITQACPKVSFEPIPIHYCAPAGFAILKCKDKEFNGTGPCKNVSTVQCTHGIKPVVSTQLL
LNGSLAEEEVIIRSENITNNAKTIIVQLTKPVKINCTRPNNNTRKSIRIGPGQAFYATGDIIGDIRQAHCNVSRSEWNKTLQKVA
KQLRKYFKNKTIIFTNSSGGDLEITTHSFNCGGEFFYCNTSGLFNSTWNNGTMKNTITLPCRIKQIINMWQRAGQAMYAPPIQGV
IRCESNITGLLLTRDGGNNNTNETFRPGGGDMRDNWRSELYKYKVVKIEPLGVAPTRAKRRVVEREKRAVGIGAVFLGFLGAAGS
TMGAASITLTVQARQLLSGIVQQQSNLLRAIEAQQHLLKLTVWGIKQLQARVLAVERYLKDQQLLGIWGCSGKLICTTNVPWNSS
WSNKSQNEIWDNMTWLQWDKEISNYTHIIYNLIEESQNQQEKNEQDLLALDKWANLWNWFDISNWLWYIKIFIMIVGGLIGLRIV
FAVLSVINRVRQGYSPLSFQTHTPNPRGLDRPGRIEEEGGEQGRDRSIRLVSGFLALAWDDLRSLCLFSYHRLRDFILIAARTVE
LLGHSSLKGLRLGWEGLKYLWNLLLYWGRELKISAINLVDTIAIAVAGWTDRVIEIGQRIGRAILHIPRRIRQGLERALL
*Amino acid sequence underlined is the fusion domain that will be deleted in 140CF design and the "W" underlined with red color is the last amino acid at the C terminus, and all the remaining amino acids after the "W" will be deleted in 140CF design.

Con-A1-2003 140CF.pep (629 a.a.)
Nick name: 001

MRVMGIQRNCQHLLRWGTMILGMIIICSAAENLWVTVYYGVPVWKDAETTLFCASDAKAYETEMHNVWATHACVPTDPNPQEIHL
ENVTEEFNMWKNNMVEQMHTDIISLWDQSLKPCVKLTPLCVTLNCSNVNVTNNTTNTHEEEIKNCSFNMTTELRDKKQKVYSLFY
RLDVVQINENNSNSSYRLINCNTSAITQACPKVSFEPIPIHYCAPAGFAILKCKDKEFNGTGPCKNVSTVQCTHGIKPVVSTQLL
LNGSLAEEEVIIRSENITNNAKTIIVQLTKPVKINCTRPNNNTRKSIRIGPGQAFYATGDIIGDIRQAHCNVSRSEWNKTLQKVA
KQLRKYFKNKTIIFTNSSGGDLEITTHSFNCGGEFFYCNTSGLFNSTWNNGTMKNTITLPCRIKQIINMWQRAGQAMYAPPIQGV
IRCESNITGLLLTRDGGNNNTNETFRPGGGDMRDNWRSELYKYKVVKIEPLGVAPTRAK**TLTVQARQLLSGIVQQQSNLLRAIEA**
QQHLLKLTVWGIKQLQARVLAVERYLKDQQLLGIWGCSGKLICTTNVPWNSSWSNKSQNEIWDNMTWLQWDKEISNYTHIIYNLI
EESQNQQEKNEQDLLALDKWANLWNWFDISNWLW*

*Amino acids seen in blue color is for easy identification of the junction of the deleted fusion cleavage site.

CODON-OPTIMIZED Con-A1-2003.seq
Nick name: 001 (1918 nt)

TTCAGTCGACAGCCACCATGAGGGTGATGGGAATCCAACGGAACTGCCAGCATCTTCTCCGGTGGGGAACGATGATACTGGGAAT
GATAATAATCTGCTCTGCCGCTGAAAACCTCTGGGTCACAGTGTACTACGGAGTGCCTGTATGGAAGGACGCTGAAACCACTCTC
TTTTGTGCTTCCGATGCTAAAGCCTACGAAACCGAGATGCACAATGTTTGGGCCACCCACGCCTGCGTGCCAACTGATCCTAATC
CACAAGAAATACATCTGGAGAATGTTACTGAGGAATTTAACATGTGGAAAAATAATATGGTAGAGCAAATGCACACTGACATCAT
TTCACTCTGGGACCAATCACTCAAACCCTGCGTTAAACTTACCCCCCTCTGCGTGACCCTCAATTGTAGCAACGTCAACGTCACA
AATAATACAACCAACACTCACGAGGAAGAAATTAAAAATTGCTCCTTTAATATGACCACTGAACTTCGCGACAAAAAACAAAAAG
TCTATTCACTGTTTTATAGGCTGGACGTCGTCCAAATCAACGAGAACAATTCTAACAGTAGCTATCGACTTATCAATTGCAATAC
CTCTGCTATTACCCAAGCTTGTCCTAAAGTCTCTTTTGAACCAATCCCTATCCACTACTGTGCCCCAGCTGGATTCGCAATTCTG
AAGTGCAAGGATAAGGAATTCAACGGAACTGGCCCTTGCAAGAACGTTAGCACTGTCCAATGCACTCACGGAATCAAACCAGTAG
TCAGCACTCAACTGCTCCTGAATGGCTCACTCGCCGAAGAAGAGGTGATTATCCGAAGCGAGAACATAACTAACAATGCGAAGAC
AATAATTGTTCAATTGACGAAACCAGTGAAGATCAACTGTACTAGACCAAATAACAACACAAGAAAATCTATCAGAATTGGCCCC
GGACAAGCCTTCTACGCAACAGGAGATATCATAGGTGACATCAGACAGGCCCATTGCAACGTTTCAAGAAGCGAGTGGAATAAAA
CACTCCAGAAAGTGGCAAAGCAGCTGAGAAAATACTTTAAGAACAAGACAATCATATTTACTAACTCCTCCGGAGGTGATCTCGA
AATAACCACTCATAGCTTTAATTGTGGGGGCGAATTCTTCTACTGTAACACATCTGGCCTCTTTAATTCTACCTGGAATAACGGC
ACCATGAAAAATACTATCACCCTCCCTTGCAGAATTAAGCAAATCATTAACATGTGGCAGAGAGCAGGACAGGCCATGTATGCCC
CTCCCATTCAAGGTGTGATTCGATGTGAAAGCAACATTACTGGACTTCTTCTGACCCGGGATGGCGGAAATAATAATACCAATGA
GACATTCAGACCCGGCGGCGGCGATATGCGAGACAATTGGCGAAGTGAACTTTATAAATACAAAGTAGTTAAGATTGAGCCCCTT
GGAGTTGCCCCTACTAGAGCAAAAACATTGACCGTTCAGGCCAGGCAGCTGCTCTCAGGAATCGTGCAGCAGCAAAGTAACCTCC
TCCGAGCTATCGAGGCACAACAACATCTCTTGAAATTGACCGTATGGGGAATCAAGCAATTGCAGGCTAGGGTTTTGGCTGTGGA
ACGCTATCTCAAGGATCAGCAGCTTCTGGGAATCTGGGGATGCTCTGGGAAATTGATATGTACTACAAACGTACCCTGGAACTCA
AGCTGGAGTAATAAAAGCCAGAACGAAATTTGGGATAATATGACCTGGCTGCAGTGGGACAAAGAAATTTCTAATTATACTCATA
TCATATACAATCTGATCGAAGAATCACAGAACCAGCAGGAAAAGAATGAGCAAGACCTTCTGGCCTTGGACAAGTGGGCTAACTT
GTGGAACTGGTTTGACATTAGCAACTGGCTGTGGTAAAGATCTTACAA

CONSENSUS_C-2003 (835 a.a)

MRVRGILRNCQQWWIWGILGFWMLMICNVVGNLWVTVYYGVPVWKEAKTTLFCASDAKAYEKEVHNVWATHACVPTDPNPQEIVL
ENVTENFNMWKNDMVDQMHEDIISLWDQSLKPCVKLTPLCVTLNCTNATNATNTMGEIKNCSFNITTELRDKKQKVYALFYRLDI
VPLNENNSYRLINCNTSAITQACPKVSFDPIPIHYCAPAGYAILKCNNKTFNGTGPCNNVSTVQCTHGIKPVVSTQLLLNGSLAE
EEIIIRSENLTNNAKTIIVHLNESVEIVCTRPNNNTRKSIRIGPGQTFYATGDIIGDIRQAHCNISEDKWNKTLQKVSKKLKEHF
PNKTIKFEPSSGGDLEITTHSFNCRGEFFYCNTSKLFNSTYNSTNSTITLPCRIKQIINMWQEVGRAMYAPPIAGNITCKSNITG
LLLTRDGGKNNTETFRPGGGDMRDNWRSELYKYKVVEIKPLGIAPTKAKRRVVEREKRAVGIGAVFLGFLGAAGSTMGAASITLT
VQARQLLSGIVQQQSNLLRAIEAQQHMLQLTVWGIKQLQTRVLAIERYLKDQQLLGIWGCSGKLICTTAVPWNSSWSNKSQEDIW
DNMTWMQWDREISNYTDTIYRLLEDSQNQQEKNEKDLLALDSWKNLWNWFDITNWLWYIKIFIMIVGGLIGLRIIFAVLSIVNRV
RQGYSPLSFQTLTPNPRGPDRLGRIEEEGGEQDRDRSIRLVSGFLALAWDDLRSLCLFSYHRLRDFILIAARAVELLGRSSLRGL
QRGWEALKYLGSLVQYWGLELKKSAISLLDTIAIAVAEGTDRIIELIQRICRAIRNIPRRIRQGFEAALQ

*Amino acid sequence underlined is the fusion domain that will be deleted in 140CF design and the "W" underlined with red color is the last amino acid at the C terminus, and all the remaining amino acids after the "W" will be deleted in 140CF design..

Con-C 2003 140CF.pep (619 a.a.)
Nick name: 003

MRVRGILRNCQQWWIWGILGFWMLMICNVVGNLWVTVYYGVPVWKEAKTTLFCASDAKAYEKEVHNVWATHACVPTDPNPQEIVL
ENVTENFNMWKNDMVDQMHEDIISLWDQSLKPCVKLTPLCVTLNCTNATNATNTMGEIKNCSFNITTELRDKKQKVYALFYRLDI
VPLNENNSYRLINCNTSAITQACPKVSFDPIPIHYCAPAGYAILKCNNKTFNGTGPCNNVSTVQCTHGIKPVVSTQLLLNGSLAE
EEIIIRSENLTNNAKTIIVHLNESVEIVCTRPNNNTRKSIRIGPGQTFYATGDIIGDIRQAHCNISEDKWNKTLQKVSKKLKEHF
PNKTIKFEPSSGGDLEITTHSFNCRGEFFYCNTSKLFNSTYNSTNSTITLPCRIKQIINMWQEVGRAMYAPPIAGNITCKSNITG
LLLTRDGGKNNTETFRPGGGDMRDNWRSELYKYKVVEIKPLGIAPTKAK**TLTVQARQLLSGIVQQQSNLLRAIEAQQHMLQLTVW**
GIKQLQTRVLAIERYLKDQQLLGIWGCSGKLICTTAVPWNSSWSNKSQEDIWDNMTWMQWDREISNYTDTIYRLLEDSQNQQEKN
EKDLLALDSWKNLWNWFDITNWLW*

*Amino acids seen in blue color is for easy identification of the junction of the deleted fusion cleavage site.

CODON-OPTIMIZED Con-C-2003 140CF (1,888 nt.)
Nick name:003

TTCAGTCGACAGCCACCATGCGAGTGAGAGGCATTCTGCGGAATTGTCAGCAATGGTGGATCTGGGGCATACTCGGATTCTGGAT
GCTTATGATATGCAATGTTGTGGGGAACCTGTGGGTTACCGTATACTATGGGGTTCCAGTCTGGAAGGAGGCTAAAACAACGCTG
TTCTGTGCAAGTGACGCCAAAGCCTACGAGAAAGAAGTGCACAACGTCTGGGCTACCCACGCTTGTGTTCCAACCGATCCAAACC
CCCAGGAAATCGTCCTCGAGAACGTGACTGAAAACTTTAACATGTGGAAGAATGATATGGTAGATCAGATGCACGAAGATATCAT
TTCATTGTGGGACCAATCATTGAAACCATGCGTAAAACTGACCCCCCTCTGCGTAACACTTAACTGCACCAATGCAACTAATGCC
ACCAATACTATGGGCGAAATAAAAAACTGTAGCTTTAACATTACAACGGAACTCCGGGATAAGAAACAAAAGGTCTACGCGCTCT
TTTACCGACTCGATATCGTCCCACTTAACGAGAATAATAGTTACCGCCTGATTAACTGTAACACATCAGCCATTACGCAAGCTTG
CCCCAAAGTTTCTTTCGACCCCATCCCAATTCACTATTGTGCCCCCGCTGGATACGCTATACTTAAATGCAACAATAAAACATTT
AATGGAACCGGACCATGTAACAACGTCAGTACCGTACAATGTACGCACGGAATTAAACCTGTTGTCTCAACCCAGCTTCTCCTTA
ACGGCTCATTGGCGGAGGAAGAAATTATTATCAGATCAGAAAACTTGACCAACAATGCCAAAACCATCATCGTGCACCTCAATGA
ATCCGTGGAAATCGTGTGCACCAGACCAAATAACAATACCCGGAAATCAATCAGGATTGGGCCTGGCCAGACATTTTACGCTACA
GGTGATATAATTGGCGATATTAGACAAGCCCATTGCAACATATCAGAAGACAAGTGGAATAAGACTCTGCAGAAGGTTTCTAAGA
AGCTGAAGGAACACTTTCCCAATAAAACGATTAAGTTCGAGCCCTCTTCAGGAGGAGACCTTGAGATCACAACACACTCTTTTAA
TTGTAGAGGGGAGTTCTTCTATTGTAATACATCAAAGCTCTTTAACAGTACCTACAACTCCACTAATAGTACCATCACACTCCCC
TGCAGAATAAAGCAAATAATCAACATGTGGCAAGAAGTTGGCCGAGCAATGTACGCCCCTCCCATCGCAGGCAACATTACATGTA
AATCCAATATTACTGGCCTTTTGCTGACACGGGACGGCGGAAAGAATAACACTGAGACCTTCAGACCTGGCGGAGGCGATATGCG
CGATAATTGGCGGAGCGAGCTCTACAAGTATAAAGTCGTTGAAATCAAGCCACTGGGCATAGCTCCTACGAAAGCAAAGACACTC
ACTGTTCAGGCTAGACAGCTGCTCTCCGGCATAGTGCAACAGCAATCCAATCTCCTGCGAGCTATCGAAGCCCAACAACATATGC
TCCAGCTTACCGTCTGGGGAATCAAACAATTGCAAACACGAGTGCTGGCGATAGAGAGATATTTGAAAGATCAGCAACTCCTGGG
GATTTGGGGCTGTTCAGGTAAGCTCATCTGTACAACTGCGGTGCCGTGGAACTCAAGCTGGAGTAACAAAAGCCAAGAGGATATA
TGGGACAACATGACTTGGATGCAGTGGGATCGAGAAATAAGCAACTATACAGATACCATTTATCGGCTCCTGGAGGACTCACAGA
ACCAGCAGGAGAAAAATGAGAAAGATTTGCTCGCGCTTGACAGTTGGAAGAATTTGTGGAATTGGTTCGACATTACAAACTGGCT
CTGGTAAAGATCTTACAA

Fig. 3Z

CONSENSUS_G-2003 (842 a.a.)

MRVKGIQRNWQHLWKWGTLILGLVIICSASNNLWVTVYYGVPVWEDADTTLFCASDAKAYSTERHNVWATHACVPTDPNPQEITL
ENVTENFNMWKNNMVEQMHEDIISLWDESLKPCVKLTPLCVTLNCTDVNVTNNNTNNTKKEIKNCSFNITTEIRDKKKKEYALFY
RLDVVPINDNGNSSIYRLINCNVSTIKQACPKVTFDPIPIHYCAPAGFAILKCRDKKFNGTGPCKNVSTVQCTHGIKPVVSTQLL
LNGSLAEEEIIIRSENITDNTKVIIVQLNETIEINCTRPNNNTRKSIRIGPGQAFYATGDIIGDIRQAHCNVSRTKWNEMLQKVK
AQLKKIFNKSITFNSSSGGDLEITTHSFNCRGEFFYCNTSGLFNNSLLNSTNSTITLPCKIKQIVRMWQRVGQAMYAPPIAGNIT
CRSNITGLLLTRDGGNNNTETFRPGGGDMRDNWRSELYKYKIVKIKPLGVAPTRARRRVVEREKRAVGLGAVLLGFLGAAGSTMG
AASITLTVQVRQLLSGIVQQQSNLLRAIEAQQHLLQLTVWGIKQLQARVLAVERYLKDQQLLGIWGCSGKLICTTNVPWNTSWSN
KSYNEIWDNMTWIEWEREISNYTQQIYSLIEESQNQQEKNEQDLLALDKWASLWNWFDITKWLWYIKIFIMIVGGLIGLRIVFAV
LSIVNRVRQGYSPLSFQTLTHHQREPDRPERIEEGGGEQDKDRSIRLVSGFLALAWDDLRSLCLFSYHRLRDFILIAARTVELLG
RSSLKGLRLGWEGLKYLWNLLLYWGQELKNSAINLLDTIAIAVANWTDRVIEVAQRACRAILNIPRRIRQGLERALL

*Amino acid sequence underlined is the fusion domain that will be deleted in 140CF design and the "W" underlined with red color is the last amino acid at the C terminus, and all the remaining amino acids after the "W" will be deleted in 140CF design.

Con-G-2003 140CF (626 a.a.)
Nick name: 007

MRVKGIQRNWQHLWKWGTLILGLVIICSASNNLWVTVYYGVPVWEDADTTLFCASDAKAYSTERHNVWATHACVPTDPNPQEITL
ENVTENFNMWKNNMVEQMHEDIISLWDESLKPCVKLTPLCVTLNCTDVNVTNNNTNNTKKEIKNCSFNITTEIRDKKKKEYALFY
RLDVVPINDNGNSSIYRLINCNVSTIKQACPKVTFDPIPIHYCAPAGFAILKCRDKKFNGTGPCKNVSTVQCTHGIKPVVSTQLL
LNGSLAEEEIIIRSENITDNTKVIIVQLNETIEINCTRPNNNTRKSIRIGPGQAFYATGDIIGDIRQAHCNVSRTKWNEMLQKVK
AQLKKIFNKSITFNSSSGGDLEITTHSFNCRGEFFYCNTSGLFNNSLLNSTNSTITLPCKIKQIVRMWQRVGQAMYAPPIAGNIT
CRSNITGLLLTRDGGNNNTETFRPGGGDMRDNWRSELYKYKIVKIKPLGVAPTRAR**TLTVQVRQLLSGIVQQQSNLLRAIEAQQH
LLQLTVWGIKQLQARVLAVERYLKDQQLLGIWGCSGKLICTTNVPWNTSWSNKSYNEIWDNMTWIEWEREISNYTQQIYSLIEES
QNQQEKNEQDLLALDKWASLWNWFDITKWLW***

*Amino acids seen in blue color is for easy identification of the junction of the deleted fusion cleavage site

CODON-OPTIMIZED Con-G-2003 140CF.seq
Nick name:007

TTCAGTCGACAGCCACCATGCGAGTGAAGGGAATCCAGAGAAATTGGCAGCACCTTTGGAAGTGGGGCACACTCATCCTCGGCCT
TGTGATCATATGCTCTGCCTCAAATAACCTTTGGGTCACAGTTTATTACGGCGTGCCCGTTTGGGAGGACGCAGACACAACTCTT
TTTTGTGCCAGCGACGCTAAGGCTTATTCAACAGAGAGGCATAACGTTTGGGCTACACATGCATGCGTGCCGACCGATCCTAATC
CCCAGGAAATCACTCTTGAGAATGTTACAGAGAATTTTAATATGTGGAAGAACAACATGGTTGAACAGATGCATGAAGACATAAT
TTCTCTCTGGGATGAATCTCTGAAACCTTGCGTGAAGCTTACACCACTGTGCGTTACCCTGAATTGCACTGACGTCAATGTCACA

AATAATAATACCAACAATACAAAAAAAGAAATCAAAAATTGTTCTTTCAACATAACCACCGAGATACGCGATAAAAAAAAGAAAG
AATACGCCCTGTTCTACAGACTCGATGTGGTCCCAATTAATGACAACGGAAATTCTTCCATCTACCGACTTATCAATTGTAACGT
GTCTACAATCAAACAGGCCTGTCCTAAAGTCACATTTGACCCTATTCCCATTCATTACTGTGCCCCCGCTGGCTTCGCTATTCTT
AAATGCCGAGACAAAAAATTTAACGGAACAGGACCATGCAAGAATGTCTCAACAGTTCAATGCACTCATGGAATTAAACCAGTCG
TTTCTACTCAACTCCTTCTCAATGGAAGCCTGGCAGAAGAGGAAATCATAATCCGCAGCGAAAACATAACCGACAACACAAAAGT
AATCATCGTACAGCTGAACGAGACCATTGAAATAAATTGTACGAGACCTAATAATAACACAAGAAAAAGCATACGCATCGGCCCC
GGACAGGCTTTCTACGCCACAGGAGACATTATCGGAGATATCCGCCAGGCTCACTGTAATGTGTCTAGAACAAAATGGAACGAAA
TGCTTCAGAAGGTCAAAGCTCAGCTCAAGAAAATATTCAACAAATCTATTACATTCAACTCATCATCAGGCGGCGATCTGGAGAT
AACAACTCATTCCTTCAACTGTCGGGGAGAATTTTTTTACTGTAACACGTCCGGCCTGTTCAACAATTCACTCCTGAATAGCACT
AACTCCACCATCACTCTCCCATGTAAGATCAAACAAATCGTCAGAATGTGGCAGCGAGTCGGTCAAGCTATGTACGCCCCTCCAA
TCGCCGGTAATATCACATGTAGAAGCAATATCACAGGGCTCTTGCTTACAAGGGACGGCGGGAACAACAACACCGAAACCTTCAG
ACCAGGAGGAGGAGACATGCGAGACAATTGGCGGAGCGAGCTGTATAAATATAAGATCGTAAAAATCAAACCATTGGGTGTAGCG
CCAACTAGAGCCCGAACACTGACCGTGCAGGTGAGGCAACTGCTGAGCGGCATTGTCCAACAACAATCCAATCTTCTTAGAGCAA
TCGAGGCCCAGCAGCATCTGCTCCAGCTTACTGTATGGGGAATCAAACAACTGCAAGCAAGAGTATTGGCAGTGGAGAGGTATCT
CAAGGACCAGCAGCTTCTGGGAATTTGGGGTTGCAGCGGAAAGCTCATATGTACAACCAATGTGCCCTGGAACACTAGTTGGAGT
AATAAGAGTTACAATGAAATCTGGGACAATATGACATGGATCGAATGGGAGCGCGAAATATCCAACTATACTCAGCAAATCTATT
CCCTCATTGAAGAGAGTCAGAACCAGCAGGAAAAGAATGAGCAAGACCTCCTCGCCCTGGATAAATGGGCATCTCTGTGGAACTG
GTTTGACATAACTAAATGGTTGTGGTAAAGATCTTACAA

Fig. 33

A **CONSENSUS_01_AE-2003 (854 a.a.)**

MRVKETQMNWPNLWKWGTLILGLVIICSASDNLWVTVYYGVPVWRDADTTLFCASDAKAHETEVHNVWATHACVPTDPNPQEIHL
ENVTENFNMWKNNMVEQMQEDVISLWDQSLKPCVKLTPLCVTLNCTNANLTNVNNITNVSNIIGNITNEVRNCSFNMTTELRDKK
QKVHALFYKLDIVQIEDNNSYRLINCNTSVIKQACPKISFDPIPIHYCTPAGYAILKCNDKNFNGTGPCKNVSSVQCTHGIKPVV
STQLLLNGSLAEEEIIIRSENLTNNAKTIIVHLNKSVEINCTRPSNNTRTSITIGPGQVFYRTGDIIGDIRKAYCEINGTKWNEV
LKQVTEKLKEHFNNKTIIFQPPSGGDLEITMHHFNCRGEFFYCNTTKLFNNTCIGNETMEGCNGTIILPCKIKQIINMWQGAGQA
MYAPPISGRINCVSNITGILLTRDGGANNTNETFRPGGGNIKDNWRSELYKYKVVQIEPLGIAPTRAKRRVVEREKRAVGIGAMI
FGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLRAIEAQQHLLQLTVWGIKQLQARVLAVERYLKDQKFLGLWGCSGKIIC
TTAVPWNSTWSNRSFEEIWNNMTWIEWEREISNYTNQIYEILTESQNQQDRNEKDLLELDKWASLWNWFDITNWLWYIKIFIMIV
GGLIGLRIIFAVLSIVNRVRQGYSPLSFQTPTHHQREPDRPERIEEGGGEQGRDRSVRLVSGFLALAWDDLRSLCLFSYHRLRDF
ILIAARTVELLGHSSLKGLRRGWEGLKYLGNLLLYWGQELKISAISLLDATAIAVAGWTDRVIEVAQGAWRAILHIPRRIRQGLE
RALL

*Amino acid sequence underlined is the fusion domain that will be deleted in 140CF design and the "W" underlined with red color is the last amino acid at the C terminus, and all the remaining amino acids after the "W" will be deleted as 140CF.

B **Con-AE01-2003 140CF.pep (638 a.a.)**
Nick name: 008

MRVKETQMNWPNLWKWGTLILGLVIICSASDNLWVTVYYGVPVWRDADTTLFCASDAKAHETEVHNVWATHACVPTDPNPQEIHL
ENVTENFNMWKNNMVEQMQEDVISLWDQSLKPCVKLTPLCVTLNCTNANLTNVNNITNVSNIIGNITNEVRNCSFNMTTELRDKK
QKVHALFYKLDIVQIEDNNSYRLINCNTSVIKQACPKISFDPIPIHYCTPAGYAILKCNDKNFNGTGPCKNVSSVQCTHGIKPVV
STQLLLNGSLAEEEIIIRSENLTNNAKTIIVHLNKSVEINCTRPSNNTRTSITIGPGQVFYRTGDIIGDIRKAYCEINGTKWNEV
LKQVTEKLKEHFNNKTIIFQPPSGGDLEITMHHFNCRGEFFYCNTTKLFNNTCIGNETMEGCNGTIILPCKIKQIINMWQGAGQA
MYAPPISGRINCVSNITGILLTRDGGANNTNETFRPGGGNIKDNWRSELYKYKVVQIEPLGIAPTRAK**TLTVQARQLLSGIVQQQ**
SNLLRAIEAQQHLLQLTVWGIKQLQARVLAVERYLKDQKFLGLWGCSGKIICTTAVPWNSTWSNRSFEEIWNNMTWIEWEREISN
YTNQIYEILTESQNQQDRNEKDLLELDKWASLWNWFDITNWLW*

*Amino acids seen in blue color is for easy identification of the junction of the deleted fusion cleavage site.

C **CODON-OPTIMIZED Con-AE01-2003 140CF.seq (1945 nt.)**
Nick name: 008

ttcagtcgacagccaccATGCGAGTCAAGGAAACACAAATGAACTGGCCTAATCTGTGGAAGTGGGGCACCCTGATCCTGGGTTT
GGTCATTATTTGCTCTGCGAGCGACAATCTCTGGGTTACTGTCTATTACGGAGTCCCCGTTTGGAGAGATGCCGACACTACACTG
TTCTGCGCCTCAGATGCCAAAGCTCATGAAACTGAAGTGCATAATGTTTGGGCAACCCACGCCTGTGTTCCTACCGACCCAAACC
CCCAAGAAATACACCTGGAAAACGTGACCGAGAACTTTAATATGTGGAAGAATAACATGGTTGAACAGATGCAAGAAGACGTAAT
CAGCCTGTGGGATCAAAGTCTGAAACCTTGCGTAAAACTGACTCCACTTTGCGTAACACTTAATTGCACCAACGCGAACCTGACA
AACGTTAACAACATCACTAACGTCTCCAACATCATCGGCAACATAACGAACGAAGTGAGAAATTGCAGTTTCAATATGACTACAG
AGCTCCGGGACAAGAAACAGAAGGTCCATGCTCTCTTTTACAAACTCGACATCGTCCAGATCGAAGACAATAACAGCTACAGACT
TATAAATTGTAATACATCCGTGATTAAACAAGCATGCCCCAAAATAAGCTTCGATCCTATTCCTATCCACTACTGTACTCCTGCC
GGCTATGCTATCTTGAAATGCAATGATAAGAACTTCAATGGGACCGGACCTTGTAAGAACGTGTCTAGTGTGCAATGCACTCACG
GCATTAAACCAGTGGTAAGCACCCAGCTGCTCCTGAACGGCTCTCTGGCAGAGGAAGAGATTATTATTCGAAGTGAGAACCTCAC
CAACAACGCTAAGACTATCATCGTACATCTCAATAAATCAGTCGAAATTAATTGCACCAGACCCTCCAATAATACTAGAACTTCA
ATCACTATCGGCCCAGGACAAGTCTTTTATAGAACAGGAGATATCATAGGAGATATCAGAAAGGCATATTGCGAGATAAACGGGA
CAAAATGGAACGAAGTACTCAAACAAGTCACAGAGAAGCTTAAGGAACATTTCAACAATAAAACCATTATTTTTCAACCCCCAAG
TGGCGGAGACCTCGAAATCACTATGCACCACTTCAACTGCCGCGGCGAATTTTTTTATTGCAATACCACTAAACTTTTCAACAAT

ACGTGCATCGGAAATGAGACCATGGAGGGCTGCAATGGAACAATCATACTCCCATGCAAGATAAAACAAATCATTAACATGTGGC
AAGGTGCTGGACAAGCTATGTATGCACCCCCAATATCCGGTAGAATTAATTGCGTCAGCAACATCACTGGCATACTGCTCACTAG
AGACGGAGGAGCAAATAATACAAATGAAACATTCCGACCAGGCGGCGGCAACATTAAGGACAACTGGCGGTCCGAACTCTATAAG
TACAAAGTCGTACAGATCGAACCTCTTGGAATAGCACCGACTCGCGCTAAGACACTCACAGTACAGGCCCGACAACTTCTTTCTG
GAATCGTACAGCAGCAATCCAACCTCCTCCGCGCAATCGAGGCCCAACAACATCTGCTTCAGCTCACAGTTTGGGGAATCAAGCA
GCTCCAGGCACGCGTGCTCGCAGTGGAAAGATACCTGAAGGATCAGAAATTCCTTGGTCTCTGGGGATGTTCTGGCAAAATAATC
TGCACTACCGCGGTTCCCTGGAATTCAACATGGAGCAACCGGAGTTTTGAAGAGATATGGAACAATATGACATGGATAGAGTGGG
AAAGGGAAATTAGTAACTATACGAACCAGATATACGAAATCCTCACCGAAAGCCAAAATCAGCAGGATCGCAACGAAAAAGACCT
CCTCGAGCTTGATAAGTGGGCATCCCTTTGGAACTGGTTCGACATCACAAATTGGCTCTGGtaaagatcttacaa

934

Wild-type subtype A Env

A **00KE_MSA4076-A (Subtype A, 891 a.a)**

MGAMGIQMNWQNLWRWGTMILGMLIICSVAEKSWVTVYYGVPVWRDAETTLFCASDAKAHDKEVHNVWATHACVPTDPNPQEMIL
ENVTEDFNMWKNSMVEQMHTDIISLWDQSLKPCVKLTPLCVTLNCSDSNITSNSTSNSTKDSATLDMKSEIQNCSFNMTTELRDK
KQKVYSLFYRLDVVQINENSSDYRLINCNTSAITQACPKVTFEPIPIHYCAPAGFAILKCNDKKFNGTGPCTNVSTVQCTHGIKP
VVTTQLLLNGSLAEEEVMIRSENITENAKNIIVQFKEPVQIICIRPGNNTRKSVHIGPGQAFYATGDIIGDIRQAHCNVSRELWN
KTLQEVATQLRKHFRNNTKIIFTNSSGGDVEITTHSFNCGGEFFYCDTSGLFNSSWTASNDSMQEAHSTESNITLQCRIKQIINM
WQRAGQAMYAPPIPGIIRCESNITGLILTRDGGEGNNSTNETFRPVGGNMRDNWRSELYKYKVVKVEPLGVAPTKSRRRVVEREK
RAVGLGAVFIGFLGAAGSTMGAASMTLTVQARQLLSGIVQQQSNLLRAIEAQQHLLKLTVWGIKQLQARVLAVERYLRDQQLLGI
WGCSGKLICTTNVPWNSSWSNKSLDEIWENMTWMQWDKEVSNYTQMIYNLLEESQNQQEKNEQELLALDKWANLWNWFNISNWLW
YIKIFIMIVGGLIGLRIVFAVLSVINRVRQGYSPLSFQTHTPNPRGLDRPGRIEEEGGEQDRDRSIRLVSGFLALAWDDLRSLCL
FSYHRLRDFILIAARTLELLGHNSLKGLRLGWEGLKYLWNLLAYWGRELKISAISLVDSIAIAVAGWTDRIIEIVQAIGRAILHI
PRRIRQGLERALI

*Amino acid sequence underlined is the fusion domain that will be deleted in 140CF design and the "W" underlined with red color is the last amino acid at the C terminus, and all the remaining amino acids after the "W" will be deleted in 140CF design.

B **00KE_MSA4076-A 140CF.pep (647 a.a)**

Nick name: 011

MGAMGIQMNWQNLWRWGTMILGMLIICSVAEKSWVTVYYGVPVWRDAETTLFCASDAKAHDKEVHNVWATHACVPTDPNPQEMIL
ENVTEDFNMWKNSMVEQMHTDIISLWDQSLKPCVKLTPLCVTLNCSDSNITSNSTSNSTKDSATLDMKSEIQNCSFNMTTELRDK
KQKVYSLFYRLDVVQINENSSDYRLINCNTSAITQACPKVTFEPIPIHYCAPAGFAILKCNDKKFNGTGPCTNVSTVQCTHGIKP
VVTTQLLLNGSLAEEEVMIRSENITENAKNIIVQFKEPVQIICIRPGNNTRKSVHIGPGQAFYATGDIIGDIRQAHCNVSRELWN
KTLQEVATQLRKHFRNNTKIIFTNSSGGDVEITTHSFNCGGEFFYCDTSGLFNSSWTASNDSMQEAHSTESNITLQCRIKQIINM
WQRAGQAMYAPPIPGIIRCESNITGLILTRDGGEGNNSTNETFRPVGGNMRDNWRSELYKYKVVKVEPLGVAPTKSR**TLTVQARQ**
LLSGIVQQQSNLLRAIEAQQHLLKLTVWGIKQLQARVLAVERYLRDQQLLGIWGCSGKLICTTNVPWNSSWSNKSLDEIWENMTW
MQWDKEVSNYTQMIYNLLEESQNQQEKNEQELLALDKWANLWNWFNISNWLW*

*Amino acids seen in blue color is for easy identification of the junction of the deleted fusion cleavage site.

C **CODON-OPTIMIZED 00KE_MSA4076-A 140CF.seq (1972 nt.)**

Nick name: 011

ttcagtcgacagccaccATGGGGGCAATGGGAATCCAGATGAACTGGCAGAACCTCTGGCGATGGGGCACAATGATCCTGGGTAT
GCTCATCATCTGCTCTGTTGCAGAAAAGTCATGGGTAACAGTCTACTACGGCGTACCAGTGTGGCGGGACGCCGAAACCACTCTC
TTCTGCGCCTCCGATGCCAAAGCACACGATAAAGAAGTCCACAATGTTTGGGCTACCCATGCGTGCGTGCCAACCGATCCTAACC
CACAAGAAATGATACTCGAAAACGTTACTGAAGACTTCAACATGTGGAAAAATTCTATGGTTGAACAGATGCACACCGACATAAT
ATCACTGTGGGATCAGTCTCTCAAACCCTGTGTCAAATTGACCCCCCTCTGCGTTACACTGAACTGTTCCGACTCAAATATCACT
TCTAATTCAACGAGCAATAGTACGAAAGACTCCGCAACCCTTGATATGAAAAGCGAAATACAGAACTGTTCATTTAATATGACCA
CCGAACTGAGAGATAAAAAGCAGAAGGTTTATTCTCTGTTCTATCGATTGGACGTGGTTCAGATTAACGAAAATAGCAGCGATTA
CCGACTCATTAACTGCAATACATCAGCAATCACACAGGCTTGCCCAAAGGTAACATTTGAGCCAATCCCTATTCACTACTGCGCC
CCTGCAGGATTTGCCATCCTGAAATGCAACGATAAGAAGTTTAATGGGACAGGACCCTGCACCAACGTCTCCACCGTGCAATGCA
CCCACGGCATAAAACCTGTTGTTACCACACAATTGCTGCTCAATGGATCACTTGCTGAAGAGGAAGTCATGATTCGGTCTGAAAA
CATCACTGAAAATGCCAAAAATATTATAGTTCAGTTCAAAGAACCCGTCCAGATCATTTGCATTCGCCCTGGTAACAACACTCGC
AAGTCAGTGCACATTGGGCCCGGCCAGGCTTTCTATGCAACCGGAGATATTATAGGCGACATCAGACAGGCACATTGCAACGTCA
GCCGGGAATTGTGGAACAAAACTTTGCAGGAAGTTGCTACTCAGCTGCGAAAACATTTCAGAAACAATACAAAGATTATTTTCAC
TAATTCATCAGGCGGTGACGTGGAGATCACTACCCATTCATTTAACTGTGGCGGAGAATTCTTCTATTGCGATACCTCTGGGCTC
TTTAATTCCTCATGGACTGCTAGCAACGATTCAATGCAAGAAGCACATTCCACAGAAAGTAATATCACACTGCAGTGCCGAATTA
AACAAATCATCAATATGTGGCAGCGGGCCGGTCAAGCAATGTACGCACCTCCCATCCCCGGAATTATTCGATGTGAGTCTAATAT
CACTGGCCTCATTCTGACCCGAGACGGTGGCGAAGGTAATAATTCTACAAACGAGACTTTCAGACCCGTAGGAGGCAATATGCGA
GACAATTGGCGATCCGAACTGTATAAATATAAAGTGGTGAAGGTAGAACCTCTTGGAGTGGCACCCACCAAATCACGAACCCTGA
CTGTGCAGGCACGCCAACTTCTGAGCGGAATAGTCCAACAGCAATCCAATCTTCTGAGAGCTATAGAAGCCCAGCAACACCTGCT
TAAACTTACGGTGTGGGGAATCAAACAATTGCAGGCAAGAGTGCTGGCAGTGGAACGATACTTGAGAGACCAACAACTCCTGGGA
ATCTGGGGATGTTCCGGTAAGTTGATTTGCACGACAAACGTTCCCTGGAACTCTTCCTGGTCAAACAAGAGTCTGGACGAAATAT
GGGAAAATATGACATGGATGCAGTGGGACAAGGAAGTTAGCAACTATACACAGATGATCTACAACCTCCTCGAAGAATCTCAGAA

TCAACAGGAAAAAAACGAACAAGAACTGCTCGCCCTCGATAAGTGGGCTAACCTCTGGAACTGGTTTAATATTTCAAACTGGTTG
TGGtaaagatcttacaa

135

Wild-type subtype B
QH0515.1g gp160 (861a.a)

1

MRVKEIRRNCQRLRRWGTMLLGMLMICSATEQLWVTVYYGVPVWKEATTTLFCASDAKAYVTEKHNVWATHACVPTDPNPQEVVL
ENVTENFNMWKNNMVEQMHEDIISLWEQSLKPCVKLTPLCVTLNCTDKLRNDTSGTNSSSWEKVQKGEIKNCSFNITTGIRGRVQ
EYSLFYKLDVIPIDSRNNSNNSTEFSSYRLISCNTSVITQACPKISFEPIPIHYCAPAGFAILKCNDKKFNGTGPCKNVSTVQCT
HGIKPVVSTQLLLNGSLAEEEVVIRSENFTNNVKSIIVQLNKSVVINCTRPNNNTRKSIHIGAGKALYTGEIIGDIRQAHCNLSR
AQWNNTLKQIVIKLREQFGNKTIVFNQSSGGDVEIVMHSFNCGGEFFYCNSTQLFNSTWNGNDTWNDTWKDTTNDNITLPCRIKQ
IVNMWQKVGKAMYAPPIRGQIRCSSKITGLILTRDGGTNGTNETETFRPGGGNMKDNWRSELYKYKVVKIEPLGIAPTKAKRRVV
QREKRAVGTIGAMFLGFLGAAGSTMGAASLTLTVQARLLLSGIVQQQNNLLRAIEAQQHLLQLTVWGIKQLQARVLAVERYLRDQ
QLLGIWGCSGRLICTTNVPWNTSWSNRSLNYIWDNMTWMQWDREINNYTDYIYTLLEDAQNQQEKNEQELLELDKWASLWNWFDI
TNWLWYIKIFIMIVGGLIGLRIVFAVLSIVNRVRQGYSPLSLQTHLPARRGPDRPEGIGEEGGERDRDRSVRLVHGFLALVWEDL
RSLCLFSYHRLRDLLLIVARTVEILGQRGWEALKYWWNLLLYWSLELKNSAVSLVDTIAIAVAEGTDRIIEIARRIFRAFLHIPT
RIRQGLERALL

*Amino acid sequence underlined is the fusion domain that will be deleted in 140CF design and the "W" underlined with red color is the last amino acid at the C terminus, and all the remaining amino acids after the "W" will be deleted in 140CF design

3

QH0515.1g 140CF (651a.a)
Nick name: 012

MRVKEIRRNCQRLRRWGTMLLGMLMICSATEQLWVTVYYGVPVWKEATTTLFCASDAKAYVTEKHNVWATHACVPTDPNPQEVVL
ENVTENFNMWKNNMVEQMHEDIISLWEQSLKPCVKLTPLCVTLNCTDKLRNDTSGTNSSSWEKVQKGEIKNCSFNITTGIRGRVQ
EYSLFYKLDVIPIDSRNNSNNSTEFSSYRLISCNTSVITQACPKISFEPIPIHYCAPAGFAILKCNDKKFNGTGPCKNVSTVQCT
HGIKPVVSTQLLLNGSLAEEEVVIRSENFTNNVKSIIVQLNKSVVINCTRPNNNTRKSIHIGAGKALYTGEIIGDIRQAHCNLSR
AQWNNTLKQIVIKLREQFGNKTIVFNQSSGGDVEIVMHSFNCGGEFFYCNSTQLFNSTWNGNDTWNDTWKDTTNDNITLPCRIKQ
IVNMWQKVGKAMYAPPIRGQIRCSSKITGLILTRDGGTNGTNETETFRPGGGNMKDNWRSELYKYKVVKIEPLGIAPTKAK**TLTV**
QARLLLSGIVQQQNNLLRAIEAQQHLLQLTVWGIKQLQARVLAVERYLRDQQLLGIWGCSGRLICTTNVPWNTSWSNRSLNYIWD
NMTWMQWDREINNYTDYIYTLLEDAQNQQEKNEQELLELDKWASLWNWFDITNWLW*

*Amino acids seen in blue color is for easy identification of the junction of the deleted fusion cleavage site.

C

CODON-OPTIMIZED QH0515.1g 140CF.seq (1984 nt.)
Nick name:012

ttcagtcgacagccaccATGAGAGTAAAAGAAATCAGACGCAACTGTCAGAGGTTGAGGAGATGGGGAACGATGCTCCTGGGCAT
GCTGATGATTTGCAGTGCCACCGAACAGCTTTGGGTAACCGTGTACTATGGTGTACCTGTATGGAAAGAAGCCACTACAACCCTG
TTTTGCGCGTCCGACGCAAAAGCCTACGTAACAGAAAAGCACAACGTGTGGGCCACACATGCATGCGTGCCAACAGATCCAAATC
CTCAGGAAGTCGTTCTGGAAAATGTAACAGAAAATTTTAATATGTGGAAAAACAATATGGTAGAGCAGATGCATGAAGATATCAT
CTCACTGTGGGAACAATCCTTGAAACCTTGTGTCAAACTGACCCCACTTTGCGTAACACTTAACTGTACTGATAAGCTTCGCAAT
GATACGTCCGGAACAAATTCAAGCAGCTGGGAAAAAGTGCAAAAGGGCGAAATCAAAAATTGTTCATTTAACATCACTACCGGTA
TCAGAGGGCGGGTACAGGAATATTCTCTTTTCTACAAACTCGACGTCATCCCAATCGACTCCAGAAATAACTCAAATAATAGCAC
AGAATTTAGTAGTTATCGCCTTATAAGCTGCAACACCAGCGTGATTACACAAGCGTGCCCTAAAATCTCTTTTGAGCCCATTCCT
ATTCACTACTGCGCACCAGCCGGCTTCGCCATCCTCAAATGTAACGACAAGAAATTTAACGGAACCGGACCCTGTAAGAATGTGT
CCACCGTTCAATGCACTCATGGAATCAAGCCCGTCGTTTCTACCCAACTTCTTCTCAATGGTAGCCTTGCGGAGGAGGAAGTTGT
GATTCGCTCCGAAAATTTTACAAACAACGTCAAGTCAATCATCGTCCAGCTTAATAAATCCGTCGTTATTAATTGTACAAGACCC
AACAATAACACCAGAAAATCCATTCACATAGGGGCCGGGAAAGCTCTGTATACCGGGGAAATTATTGGAGACATCAGACAAGCAC
ACTGTAACTTGAGTCGCGCCCAGTGGAACAACACATTGAAACAGATCGTGATCAAGCTCAGAGAGCAGTTCGGGAATAAGACTAT
CGTGTTTAATCAGAGCTCCGGCGGTGATGTCGAAATCGTAATGCACTCTTTTAATTGTGGGGGTGAATTTTTTTACTGCAATTCT
ACACAATTGTTTAACAGCACCTGGAACGGCAATGACACATGGAATGACACCTGGAAAGATACGACAAATGATAATATTACTCTTC
CGTGCAGAATAAAGCAAATCGTAAATATGTGGCAAAAAGTGGGCAAGGCCATGTACGCACCACCTATAAGAGGACAAATTCGCTG
TTCTTCCAAGATCACAGGTCTGATACTCACACGGGACGGAGGCACGAACGGGACAAACGAGACCGAGACCTTCCGACCAGGAGGC
GGCAACATGAAGGATAACTGGAGAAGTGAACTTTACAAGTATAAAGTGGTCAAGATTGAGCCTCTGGGTATCGCCCCTACTAAGG
CTAAAACACTCACCGTGCAGGCTAGATTGCTGCTTTCAGGGATAGTCCAACAACAGAACAACCTTCTTAGAGCCATTGAAGCACA
ACAACACTTGCTGCAGTTGACAGTGTGGGGAATTAAACAGTTGCAGGCCCGGGTTCTCGCTGTCGAACGGTATCTTAGAGATCAG
CAGCTTTTGGGTATCTGGGGGTGTTCAGGCCGCCTCATATGCACCACAAATGTCCCTTGGAATACCTCATGGAGTAACAGGTCTC
TTAATTATATTTGGGACAATATGACATGGATGCAATGGGATAGAGAAATTAATAACTACACCGACTACATCTACACACTTCTGGA
GGACGCCCAGAATCAGCAGGAGAAGAACGAGCAGGAACTCCTCGAATTGGATAAGTGGGCATCACTGTGGAATTGGTTCGATATA
ACTAATTGGCTTTGGtaaagatcttacaa

Fig. 36

Wild-type subtype C
DU123.6 gp160(854 a.a)

A

MRVKGIQRNWPQWWIWGILGFWMIIICRVVGNLWVTVYYGVPVWTEAKTTLFCASDAKAYEREVHNVWATHACVPTDPNPQEIVL
GNVTENFNMWKNDMVDQMHEDIISIWDQSLKPCVKLTPLCVTLNCTDVKVNATSNGTTTYNNSIDSMNGEIKNCSFNITTEIRDK
KQKVYALFYRPDVVPLNENSSSYILINCNTSTTTQACPKVSFDPIPIHYCAPAGYAILKCNNKTFNGTGPCHNVSTVQCTHGIKP

VVSTQLLLNGSLAEEEIIIRSENLTNNAKTIIVHLNESIEIVCTRPNNNTRKSIRIGPGQTVYATNDIIGDIRQAHCNISKTKWN
TTLEKVKEKLKEHFPSKAITFQPHSGGDLEVTTHSFNCRGEFFYCDTTKLFNESNLNTTNTTTLTLPCRIKQIVNMWQGVGRAMY
APPVEGNITCNSSITGLLLVRDGGNTSNSTPEIFRPGGGNMKDNWRSELYKYKVVEIKPLGVAPTKAKRRVVEREKRAVGIGAVL
FGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLRAIEAQQHMLQLTVWGIKQLQARVLAIERYLKDQQLLGLWGCSGKLIC
PTTVPWNSSWSNKSQTDIWDNMTWMQWDREISNYTGTIYKLLEESQNQQEKNEKDLLALDSWKNLWSWFDITNWLWYIKIFIMIV
GGLIGLRIIFGVLSIVKRVRQGYSPLSFQTLTPNPRGLDRLGRIEEEGGEQDKDRSIRLVNGFLALAWDDLRSLCLFSYHRLRDF
ILVAARAVELLGRSSLRGLQRGWEALKYLGNLVQYGGLELKRRAISLFDTIAIAVAEGTDRILEVILRIIRAIRNIPTRIRQGFE
AALL

DU123.6 140CF (638 a.a)
Nick name: 013

MRVKGIQRNWPQWWIWGILGFWMIIICRVVGNLWVTVYYGVPVWTEAKTTLFCASDAKAYEREVHNVWATHACVPTDPNPQEIVL
GNVTENFNMWKNDMVDQMHEDIISIWDQSLKPCVKLTPLCVTLNCTDVKVNATSNGTTTYNNSIDSMNGEIKNCSFNITTEIRDK
KQKVYALFYRPDVVPLNENSSSYILINCNTSTTTQACPKVSFDPIPIHYCAPAGYAILKCNNKTFNGTGPCHNVSTVQCTHGIKP
VVSTQLLLNGSLAEEEIIIRSENLTNNAKTIIVHLNESIEIVCTRPNNNTRKSIRIGPGQTVYATNDIIGDIRQAHCNISKTKWN
TTLEKVKEKLKEHFPSKAITFQPHSGGDLEVTTHSFNCRGEFFYCDTTKLFNESNLNTTNTTTLTLPCRIKQIVNMWQGVGRAMY
APPVEGNITCNSSITGLLLVRDGGNTSNSTPEIFRPGGGNMKDNWRSELYKYKVVEIKPLGVAPTKAK**TLTVQARQLLSGIVQQQ**
SNLLRAIEAQQHMLQLTVWGIKQLQARVLAIERYLKDQQLLGLWGCSGKLICPTTVPWNSSWSNKSQTDIWDNMTWMQWDREISN
YTGTIYKLLEESQNQQEKNEKDLLALDSWKNLWSWFDITNWLW*

*Amino acids seen in blue color is for easy identification of the junction of the deleted fusion cleavage site.

CODON-OPTIMIZED DU123.6 140CF.seq (1945 nt.)
Nick name: 013

ttcagtcgacagccaccATGCGCGTAAAGGGGATTCAAAGAAATTGGCCGCAATGGTGGATTTGGGGAATTCTGGGCTTTTGGAT
GATAATTATATGCCGCGTTGTCGGAAATTTGTGGGTGACTGTGTACTACGGGGTGCCCGTGTGGACTGAGGCAAAGACCACCCTG
TTCTGTGCTAGCGATGCCAAAGCCTATGAACGCGAAGTGCACAATGTTTGGGCTACTCATGCCTGTGTCCCTACCGACCCAAACC
CTCAGGAAATAGTGCTCGGCAATGTAACGGAAAACTTCAACATGTGGAAAAATGATATGGTGGATCAGATGCACGAAGACATTAT
CTCAATCTGGGACCAAAGCCTGAAACCCTGCGTTAAACTGACTCCTCTCTGCGTCACTCTCAATTGCACAGATGTCAAAGTGAAT
GCCACCTCAAACGGTACGACAACTTACAACAATTCTATTGACTCTATGAACGGCGAAATCAAAAATTGTTCCTTTAACATCACCA
CCGAGATACGCGACAAAAAGCAGAAGGTCTATGCCCTTTTTTACCGCCCCGACGTAGTCCCACTCAACGAGAATTCCAGCTCATA
CATCCTCATCAACTGCAATACATCAACTACCACACAAGCATGCCCGAAAGTTAGCTTTGATCCAATTCCTATACATTACTGCGCC
CCCGCCGGCTACGCTATACTGAAATGCAATAATAAGACTTTTAACGGGACCGGCCCATGTCACAACGTGTCAACCGTGCAATGCA
CTCATGGCATCAAGCCCGTGGTGTCAACCCAGCTGCTGCTCAATGGCTCACTTGCAGAAGAAGAAATTATTATCCGCTCTGAGAA
TCTTACTAACAATGCAAAAACGATTATCGTGCACCTTAATGAATCAATAGAAATCGTGTGTACTCGGCCCAACAATAATACTAGA
AAAAGCATTCGCATCGGACCTGGCCAGACAGTTTACGCAACTAATGACATCATCGGGGACATCCGACAGGCCCATTGCAACATTT
CTAAAACCAAGTGGAATACAACCCTGGAAAAAGTAAAGGAAAAACTTAAAGAACATTTTCCCTCTAAGGCGATCACGTTTCAACC
TCACAGTGGCGGAGACTTGGAAGTCACAACACATTCTTTTAACTGCCGCGGAGAATTTTTTTATTGTGATACAACAAAACTTTTT
AATGAATCAAATCTCAACACCACAAATACAACCACACTGACCCTCCCCTGTAGAATCAAACAAATCGTAAACATGTGGCAAGGGG
TTGGAAGGGCTATGTACGCTCCCCCCGTCGAAGGAAATATAACGTGTAACAGCAGCATCACTGGGCTGCTTCTTGTTCGAGACGG
AGGCAATACTTCTAATTCAACTCCTGAAATTTTTAGGCCTGGCGGTGGCAATATGAAAGATAACTGGCGCTCAGAACTGTACAAA
TACAAAGTTGTTGAAATTAAGCCCCTGGGAGTCGCTCCAACCAAAGCTAAAACACTCACAGTGCAAGCAAGACAGCTCCTTTCAG
GCATCGTCCAGCAACAGTCAAATCTCCTTAGAGCAATCGAAGCCCAACAGCATATGCTCCAACTCACAGTCTGGGGGATTAAACA
GCTTCAAGCCCGCGTGCTTGCTATCGAACGCTATCTTAAAGACCAACAGCTTCTTGGCCTCTGGGGTTGTAGTGGAAAACTCATC
TGCCCCACCACCGTGCCTTGGAATAGTTCTTGGAGTAATAAATCACAGACCGATATTTGGGACAACATGACCTGGATGCAATGGG
ATAGGGAAATTTCTAATTATACTGGCACAATCTACAAACTCTTGGAAGAAAGTCAAAATCAGCAAGAAAAAAACGAAAAGGACCT
CCTCGCCCTGGACTCCTGGAAGAATCTTTGGAGCTGGTTCGACATAACTAATTGGCTGTGGtaaagatcttacaa

Fig. 37

Wild-type subtype CRF01_AE

97CNGX2F-AE (854 a.a.)

MRVKETQMNWPNLWKWGTLILGLVIICSASDNLWVTVYYGVPVWRDADTTLFCASDAKAHETEVHNVWATHACVPTDPNPQEIHL
ENVTENFNMWRNNMVEQMQEDVISLWDQSLKPCVKLTPLCVTLNCTNANWTNSNNTTNGPNKIGNITDEVKNCTFNMTTELKDKK
QKVHALFYKLDIVQINSSEYRLINCNTSVIKQACPKISFDPIPIHYCTPAGYAILKCNDKNFNGTGPCKNVSSVQCTHGIKPVVS
TQLLLNGSLAEEEIIIRSENLTNNAKTIIVHLNKSVEINCTRPSNNTRTSITMGPGQVFYRTGDIIGDIRKAYCEINGIKWNEVL
VQVTGKLKEHFNKTIIFQPPSGGDLEIITHHFSCRGEFFYCNTTKLFNNTCIGNTSMEGCNNTIILPCKIKQIINMWQGVGQAMY
APPISGRINCVSNITGILLTRDGGADNNTTNETFRPGGGNIKDNWRSELYKYKVVEIEPLGIAPTRAKRRVVEREKRAVGIGAMI
FGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLRAIEAQQHLLQLTVWGIKQLQARVLAVERYLKDQKFLGLWGCSGKIIC
TTAVPWNSSWSNKSFEEIWDNMTWIEWEREISNYTSQIYEILTESQNQQDRNEKDLLELDKWASLWNWFDITNWLWYIKIFIIIV
GSLIGLRIIFAVLSIVNRVRQGYSPLSFQTPTHHQREPDRPEEIGEGGGEQSKDRSVRLVSGFLALAWDDLRSLCLFSYHLLRDF
ILIAARTVELLGHSSLKGLRRGWEGLKYLGNLLLYWGQEIKISAISLLNATAIAVAGWTDRVIEVAQRAWRALLHIPRRIRQGLE
RALL

*Amino acid sequence underlined is the fusion domain that will be deleted in 140CF design and the "W" underlined with red color is the last amino acid at the C

terminus, and all the remaining amino acids after the "W" will be deleted in 140CF design.

3

97CNGX2F-AE 140CF.pep (629 a.a.)
Nick name: 018

MRVKETQMNWPNLWKWGTLILGLVIICSASDNLWVTVYYGVPVWRDADTTLFCASDAKAHETEVHNVWATHACVPTDPNPQEIHL
ENVTENFNMWRNNMVEQMQEDVISLWDQSLKPCVKLTPLCVTLNCTNANWTNSNNTTNGPNKIGNITDEVKNCTFNMTTELKDKK
QKVHALFYKLDIVQINSSEYRLINCNTSVIKQACPKISFDPIPIHYCTPAGYAILKCNDKNFNGTGPCKNVSSVQCTHGIKPVVS
TQLLLNGSLAEEEIIIRSENLTNNAKTIIVHLNKSVEINCTRPSNNTRTSITMGPGQVFYRTGDIIGDIRKAYCEINGIKWNEVL
VQVTGKLKEHFNKTIIFQPPSGGDLEIITHHFSCRGEFFYCNTTKLFNNTCIGNTSMEGCNNTIILPCKIKQIINMWQGVGQAMY
APPISGRINCVSNITGILLTRDGGADNNTTNETFRPGGGNIKDNWRSELYKYKVVEIEPLGIAPTRAR**TLTVQARQLLSGIVQQQ**
SNLLRAIEAQQHLLQLTVWGIKQLQARVLAVERYLKDQKFLGLWGCSGKIICTTAVPWNSSWSNKSFEEIWDNMTWIEWEREISN
YTSQIYEILTESQNQQDRNEKDLLELDKWASLWNW*

*Amino acids seen in blue color is for easy identification of the junction of the deleted fusion cleavage site.

2

CODON-OPTIMIZED 97CNGX2F-AE 140CF.seq (1921 nt.)
Nick name: 018

ttcagtcgacagccaccATGCGAGTAAAAGAGACACAAATGAATTGGCCCAATTTGTGGAAGTGGGGAACATTGATCCTGGGACT
GGTGATAATCTGTAGTGCATCCGACAATCTCTGGGTGACCGTTTACTATGGTGTACCAGTTTGGAGAGACGCTGATACCACCCTC
TTCTGTGCAAGCGACGCCAAAGCCCACGAAACTGAAGTCCATAATGTATGGGCCACCCACGCGTGCGTACCAACCGACCCTAATC
CCCAAGAGATCCACCTTGAGAATGTAACTGAGAATTTTAACATGTGGAGAAATAACATGGTGGAACAAATGCAGGAAGACGTTAT
TTCCTTGTGGGACCAGAGCCTTAAACCTTGTGTCAAATTGACTCCCCTGTGTGTGACTCTCAATTGTACAAACGCAAATTGGACC
AACAGCAACAACACTACCAACGGCCCTAACAAAATTGGCAATATTACTGATGAAGTCAAGAACTGCACTTTTAACATGACAACAG
AACTGAAGGATAAGAAACAGAAAGTCCATGCTCTGTTCTATAAGCTCGACATAGTACAAATTAATAGCTCAGAATATAGACTGAT
AAACTGCAATACTTCCGTTATCAAACAGGCCTGTCCAAAGATAAGCTTCGATCCCATCCCTATTCACTACTGCACACCAGCCGGT
TACGCTATCCTGAAATGCAACGATAAGAATTTTAACGGCACAGGTCCCTGCAAAAACGTTTCCTCTGTCCAGTGTACACACGGTA
TCAAGCCTGTAGTATCAACACAACTGCTCCTGAATGGCTCCTTGGCCGAAGAAGAGATCATCATTAGAAGTGAGAACCTGACGAA
CAACGCCAAGACTATAATAGTGCACCTCAATAAATCTGTAGAAATCAACTGTACCCGACCCTCAAACAACACTCGAACAAGTATA
ACAATGGGCCCTGGCCAAGTTTTTTACCGGACCGGCGACATAATAGGCGATATCAGAAAGGCATATTGCGAGATCAATGGCATCA
AGTGGAACGAAGTACTGGTTCAAGTAACTGGAAAACTCAAAGAACATTTTAATAAGACCATAATATTCCAGCCCCCGAGTGGCGG
CGACCTCGAGATTATCACCCATCACTTTTCTTGTAGAGGCGAATTTTTTTACTGTAACACGACCAAGCTCTTCAATAACACGTGC
ATCGGGAACACTTCTATGGAAGGATGTAATAATACCATTATACTGCCCTGTAAGATCAAGCAGATTATCAACATGTGGCAGGGAG
TAGGTCAGGCAATGTACGCACCACCGATTTCAGGACGGATCAATTGCGTATCAAATATCACCGGCATTCTGCTGACCCGGGACGG
AGGCGCAGACAACAATACCACTAACGAGACATTTAGACCTGGAGGCGGCAATATAAAGGATAATTGGAGAAGTGAGCTGTATAAA
TACAAAGTCGTAGAGATCGAACCCCTCGGCATTGCTCCAACCCGGGCCCGGACTCTCACCGTACAAGCTAGACAGCTGCTTTCTG
GCATAGTCCAACAGCAGTCAAACCTCCTCCGCGCTATTGAAGCACAACAACACCTGCTCCAGCTGACTGTGTGGGGAATCAAACA
ATTGCAAGCAAGAGTGCTCGCCGTGGAACGCTATTTGAAAGATCAGAAATTTCTTGGACTTTGGGGCTGCAGCGGCAAAATTATT
TGTACAACAGCGGTGCCTTGGAACTCATCCTGGAGTAATAAAAGCTTTGAAGAAATCTGGGACAATATGACATGGATTGAGTGGG
AGAGAGAGATTTCAAACTATACAAGCCAAATTTACGAAATACTGACAGAAAGTCAAAACCAGCAGGACAGAAATGAGAAAGACCT
GCTCGAACTGGATAAGTGGGCCTCTTTGTGGAACTGGtaaagatcttacaa

Fig. 38

Wild-type DRCBL-G (854a.a.)

A

MRVKGIQRNWQHLWNWGILILGLVIICSAEKLWVTVYYGVPVWEDANAPLFCASDAKAHSTESHNIWATHACVPTDPSPQEINMR
NVTENFNMWKNNMVEQMHEDIISLWDESLKPCVKLTPLCVTLNCTEINNNSTRNITEEYRMTNCSFNMTTELRDKKKAEYALFYR
TDVVPINEMNNENNGTNSTWYRLTNCNVSTIKQACPKVTFEPIPIHYCAPAGFAILKCVDKKFNGTGTCNNVSTVQCTHGIKPVV
STQLLLNGSLAEKDIIISSENISDNAKVIIVHLNRSVEINCTRPNNNTRRSVAIGPGQAFYTTGEVIGDIRKAHCNVSWTKWNET
LRDVQAKLQEYFINKSIEFNSSSGGDLEITTHSFNCGGEFFYCNTSGLFNNSILKSNISENNDTITLNCKIKQIVRMWQRVGQAM
YAPPIAGNITCRSNITGLILTRDGGDNNSTSEIFRPGGGDMKNNWRSELYKYKTVKIKSLGIAPTRARRRVVEREKRAVGVGAIF
LGFLGTAGSTMGAASITLTVQVRQLLSGIVQQQSNLLRAIEAQQHLLQLTVWGIKQLRARVLALERYLKDQQLLGIWGCSGKLIC
TTNVPWNTSWSNKSYNEIWENMTWIEWEREIDNYTYHIYSLIEQSQIQQEKNEQDLLALDQWASLWSWFSISNWLWYIRIFVMIV
GGLIGLRIVFAVLSIVNRVRQGYSPLSFQTLLHHQREPDRPAGIEEGGGEQDRDRSIRLVSGFLALAWDDLRSLCLFSYHRLRDF
ILIAARTVELLGRNSLKGLRLGWEALKYLWNLLLYWARELKNSAINLLDTIAIAVANWTDRVIEVAQRAGRAVLNIPRRIRQGLE
RALL

*Amino acid sequence underlined is the fusion domain that will be deleted in 140CF design and the "W" underlined with red color is the last amino acid at the C terminus, and all the remaining amino acids after the "W" will be deleted in 140CF design.

B

DRCBL-G 140CF.pep (630 a.a.)
Nick name: 017

MRVKGIQRNWQHLWNWGILILGLVIICSAEKLWVTVYYGVPVWEDANAPLFCASDAKAHSTESHNIWATHACVPTDPSPQEINMR
NVTENFNMWKNNMVEQMHEDIISLWDESLKPCVKLTPLCVTLNCTEINNNSTRNITEEYRMTNCSFNMTTELRDKKKAEYALFYR

TDVVPINEMNNENNGTNSTWYRLTNCNVSTIKQACPKVTFEPIPIHYCAPAGFAILKCVDKKFNGTGTCNNVSTVQCTHGIKPVV
STQLLLNGSLAEKDIIISSENISDNAKVIIVHLNRSVEINCTRPNNNTRRSVAIGPGQAFYTTGEVIGDIRKAHCNVSWTKWNET
LRDVQAKLQEYFINKSIEFNSSSGGDLEITTHSFNCGGEFFYCNTSGLFNNSILKSNISENNDTITLNCKIKQIVRMWQRVGQAM
YAPPIAGNITCRSNITGLILTRDGGDNNSTSEIFRPGGGDMKNNWRSELYKYKTVKIKSLGIAPTRAR**TLTVQVRQLLSGIVQQQ**
SNLLRAIEAQQHLLQLTVWGIKQLRARVLALERYLKDQQLLGIWGCSGKLICTTNVPWNTSWSNKSYNEIWENMTWIEWEREIDN
YTYHIYSLIEQSQIQQEKNEQDLLALDQWASLWSW*

*Amino acids seen in blue color is for easy identification of the junction of the deleted fusion cleavage site.

CODON-OPTIMIZED DRCBL-G 140CF.seq (1921 nt.)
Nick name: 017

ttcagtcgacagccaccATGAGAGTTAAAGGAATCCAACGCAATTGGCAACACCTTTGGAACTGGGGCATATTGATTCTTGGACT
GGTGATAATTTGTAGCGCTGAAAAACTCTGGGTAACTGTCTATTACGGCGTGCCTGTCTGGGAGGATGCCAACGCCCCCCTGTTC
TGCGCAAGTGATGCAAAGGCTCACAGCACTGAATCTCACAACATTTGGGCCACCCACGCCTGTGTGCCAACCGACCCTAGTCCTC
AGGAGATCAACATGAGAAACGTTACCGAAAATTTTAATATGTGGAAGAATAATATGGTGGAGCAAATGCACGAAGACATAATTTC
ACTCTGGGACGAGTCTCTGAAACCATGTGTGAAACTTACCCCCCTGTGCGTCACCCTGAACTGTACCGAAATCAACAATAACTCA
ACGAGAAATATCACAGAAGAATACCGAATGACTAACTGTTCCTTTAATATGACAACCGAACTGCGAGACAAAAAGAAGGCTGAAT
ACGCACTTTTCTACCGAACAGATGTTGTACCAATCAACGAGATGAACAATGAAAACAATGGAACGAACTCTACCTGGTATAGACT
GACAAACTGTAACGTTAGCACAATCAAGCAGGCCTGCCCTAAAGTCACATTCGAACCAATACCAATTCACTACTGCGCACCCGCC
GGATTCGCTATTCTTAAGTGCGTGGATAAGAAGTTTAACGGAACTGGAACCTGCAATAATGTATCTACAGTACAATGCACGCATG
GAATTAAGCCTGTCGTTTCAACCCAGTTGCTGCTGAATGGATCACTCGCAGAAAAGGATATTATTATCTCAAGCGAAAACATATC
TGATAATGCAAAGGTCATCATCGTCCACCTCAACCGCTCAGTTGAAATAAACTGCACTCGGCCTAATAATAACACAAGACGCTCT
GTCGCAATCGGCCCAGGACAAGCTTTTTACACTACCGGGGAAGTTATCGGCGACATACGGAAAGCCCACTGCAACGTTAGCTGGA
CCAAGTGGAATGAAACACTGCGCGATGTTCAAGCCAAACTTCAAGAATACTTCATAAACAAATCAATTGAGTTCAATTCTAGCTC
TGGCGGCGACCTCGAGATTACAACTCACTCCTTTAACTGCGGCGGCGAATTCTTTTATTGTAATACCTCCGGTCTCTTCAACAAC
TCTATCCTCAAAAGTAACATTTCTGAAAATAATGACACAATCACACTGAATTGCAAGATCAAGCAGATTGTTAGGATGTGGCAAC
GAGTCGGACAAGCTATGTACGCCCCACCCATCGCCGGAAATATAACGTGTCGATCAAATATCACTGGCCTCATCCTTACTAGAGA
TGGCGGAGACAATAATAGCACCAGCGAGATATTCAGACCAGGCGGAGGCGATATGAAAAACAACTGGAGGTCAGAGCTCTACAAG
TACAAAACAGTCAAAATTAAAAGCCTGGGCATTGCTCCCACTCGGGCCCGCACACTGACTGTCCAAGTCCGACAGCTCCTGTCCG
GAATCGTCCAACAACAGTCCAACTTGCTGCGCGCTATAGAGGCTCAACAACATCTCCTTCAACTGACTGTGTGGGGTATCAAACA
ATTGAGAGCAAGAGTGCTGGCGCTGGAACGGTATCTTAAGGACCAACAACTCCTGGGCATATGGGGGTGTTCCGGCAAACTGATC
TGCACAACAAATGTACCCTGGAACACCAGCTGGTCAAATAAAAGTTATAATGAGATATGGGAAAACATGACATGGATTGAATGGG
AAAGGGAAATTGACAATTATACATACCATATATACTCTCTCATCGAACAATCTCAGATACAACAGGAAAAGAATGAACAAGATTT
GTTGGCTCTTGACCAATGGGCTTCTTTGTGGAGTTGGtaaagatcttacaa

2003 Centralized HIV-1 Envelope Proteins and the Codon-Optimized Gene sequences

fig. 39A

2003 Cons Env

MRVMGIQRNCQHLWRWGILIFGMLIICSAAENLWVTVYYGVPVWKEANTTLFCASDAKAYDTEVHNVWATHACVPTDPNPQE
IVLENVTENFNMWKNNMVEQMHEDIISLWDQSLKPCVKLTPLCVTLNCTDVNATNNTTNNEEIKNCSFNITTEIRDKKKKVY
ALFYKLDVVPIDDNNSYRLINCNTSAITQACPKVSFEPIPIHYCAPAGFAILKCNDKKFNGTGPCKNVSTVQCTHGIKPVVS
TQLLLNGSLAEEEIIIRSENITNNAKTIIVQLNESVEINCTRPNNNTRKSIRIGPGQAFYATGDIIGDIRQAHCNISRTKWN
KTLQQVAKKLREHFNKTIIFNPSSGGDLEITTHSFNCGGEFFYCNTSELFNSTWNGTNNTITLPCRIKQIINMWQGVGQAMY
APPIEGKIRCTSNITGLLLTRDGGNNNTETFRPGGGDMRDNWRSELYKYKVVKIEPLGVAPTKAKRRVVEREKRAVGIGAVF
LGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLRAIEAQQHLLQLTVWGIKQLQARVLAVERYLKDQQLLGIWGCSGK
LICTTNVPWNSSWSNKSQDEIWDNMTWMEWDKEINNYTDIIYSLIEESQNQQEKNEQELLALDKWASLWNWFDITNWLWYIK
IFIMIVGGLIGLRIVFAVLSIVNRVRQGYSPLSFQTLIPNPRGPDRPEGIEEEGGEQDRDRSIRLVNGFLALAWDDLRSLCL
FSYHRLRDLILIAARTVELLGRRGWEALKYLWNLLQYWGQELKNSAISLLDTTAIAVAEGTDRVIEVVQRVCRAILNIPRRI
RQGFERALL$

2003 CON-S Env.seq.opt

B

ATGCGCGTGATGGGCATCCAGCGCAACTGCCAGCACCTGTGGCGCTGGGGCATCCTGATCTTCGGCATGCTGATCATCTGCT
CCGCCGCCGAGAACCTGTGGGTGACCGTGTACTACGGCGTGCCCGTGTGGAAGGAGGCCAACACCACCCTGTTCTGCGCCTC
CGACGCCAAGGCCTACGACACCGAGGTGCACAACGTGTGGGCCACCCACGCCTGCGTGCCCACCGACCCCAACCCCCAGGAG
ATCGTGCTGGAGAACGTGACCGAGAACTTCAACATGTGGAAGAACAACATGGTGGAGCAGATGCACGAGGACATCATCTCCC
TGTGGGACCAGTCCCTGAAGCCCTGCGTGAAGCTGACCCCCCTGTGCGTGACCCTGAACTGCACCGACGTGAACGCCACCAA
CAACACCACCAACAACGAGGAGATCAAGAACTGCTCCTTCAACATCACCACCGAGATCCGCGACAAGAAGAAGAAGGTGTAC
GCCCTGTTCTACAAGCTGGACGTGGTGCCCATCGACGACAACAACTCCTACCGCCTGATCAACTGCAACACCTCCGCCATCA
CCCAGGCCTGCCCCAAGGTGTCCTTCGAGCCCATCCCCATCCACTACTGCGCCCCCGCCGGCTTCGCCATCCTGAAGTGCAA
CGACAAGAAGTTCAACGGCACCGGCCCCTGCAAGAACGTGTCCACCGTGCAGTGCACCCACGGCATCAAGCCCGTGGTGTCC
ACCCAGCTGCTGCTGAACGGCTCCCTGGCCGAGGAGGAGATCATCATCCGCTCCGAGAACATCACCAACAACGCCAAGACCA
TCATCGTGCAGCTGAACGAGTCCGTGGAGATCAACTGCACCCGCCCCAACAACACCCGCAAGTCCATCCGCATCGGCCC
CGGCCAGGCCTTCTACGCCACCGGCGACATCATCGGCGACATCCGCCAGGCCCACTGCAACATCTCCCGCACCAAGTGGAAC
AAGACCCTGCAGCAGGTGGCCAAGAAGCTGCGCGAGCACTTCAACAAGACCATCATCTTCAACCCCTCCTCCGGCGGCGACC
TGGAGATCACCACCCACTCCTTCAACTGCGGCGGCGAGTTCTTCTACTGCAACACCTCCGAGCTGTTCAACTCCACCTGGAA
CGGCACCAACAACACCATCACCCTGCCCTGCCGCATCAAGCAGATCATCAACATGTGGCAGGGCGTGGGCCAGGCCATGTAC
GCCCCCCCCATCGAGGGCAAGATCCGCTGCACCTCCAACATCACCGGCCTGCTGCTGACCCGCGACGGCGGCAACAACAACA
CCGAGACCTTCCGCCCCGGCGGCGGCGACATGCGCGACAACTGGCGCTCCGAGCTGTACAAGTACAAGGTGGTGAAGATCGA
GCCCCTGGGCGTGGCCCCCACCAAGGCCAAGCGCCGCGTGGTGGAGCGCGAGAAGCGCGCCGTGGGCATCGGCGCCGTGTTC
CTGGGCTTCCTGGGCGCCGCCGGCTCCACCATGGGCGCCGCCTCCATCACCCTGACCGTGCAGGCCCGCCAGCTGCTGTCCG
GCATCGTGCAGCAGCAGTCCAACCTGCTGCGCGCCATCGAGGCCCAGCAGCACCTGCTGCAGCTGACCGTGTGGGGCATCAA
GCAGCTGCAGGCCCGCGTGCTGGCCGTGGAGCGCTACCTGAAGGACCAGCAGCTGCTGGGCATCTGGGGCTGCTCCGGCAAG
CTGATCTGCACCACCAACGTGCCCTGGAACTCCTCCTGGTCCAACAAGTCCCAGGACGAGATCTGGGACAACATGACCTGGA
TGGAGTGGGACAAGGAGATCAACAACTACACCGACATCATCTACTCCCTGATCGAGGAGTCCCAGAACCAGCAGGAGAAGAA
CGAGCAGGAGCTGCTGGCCCTGGACAAGTGGGCCTCCCTGTGGAACTGGTTCGACATCACCAACTGGCTGTGGTACATCAAG
ATCTTCATCATGATCGTGGGCGGCCTGATCGGCCTGCGCATCGTGTTCGCCGTGCTGTCCATCGTGAACCGCGTGCGCCAGG
GCTACTCCCCCCTGTCCTTCCAGACCCTGATCCCCAACCCCCGCGGCCCCGACCGCCCCGAGGGCATCGAGGAGGAGGGCGG
CGAGCAGGACCGCGACCGCTCCATCCGCCTGGTGAACGGCTTCCTGGCCCTGGCCTGGGACGACCTGCGCTCCCTGTGCCTG
TTCTCCTACCACCGCCTGCGCGACCTGATCCTGATCGCCGCCCGCACCGTGGAGCTGCTGGGCCGCCGCGGCTGGGAGGCCC
TGAAGTACCTGTGGAACCTGCTGCAGTACTGGGGCCAGGAGCTGAAGAACTCCGCCATCTCCCTGCTGGACACCACCGCCAT
CGCCGTGGCCGAGGGCACCGACCGCGTGATCGAGGTGGTGCAGCGCGTGTGCCGCGCCATCCTGAACATCCCCCGCCGCATC
CGCCAGGGCTTCGAGCGCGCCCTGCTGTAA

fig. 40A

2003 M. Group.AnC Env

MRVMGIQRNCQHLWRWGILIFGMLMICSAAENLWVTVYYGVPVWKEANTTLFCASDAKAYDTEVHNVWATHACVPTDPNPQE
IVLENVTENFNMWKNNMVEQMHEDIISLWDQSLKPCVKLTPLCVTLNCTDVNATNNSTNMGEIKNCSFNITTEIRDKKQKVY
ALFYRLDVVPINDNNSYRLINCNTSAITQACPKVSFEPIPIHYCAPAGFAILKCNDKKFNGTGPCKNVSTVQCTHGIKPVVS
TQLLLNGSLAEEEIIIRSENITDNAKTIIVQLNESVEINCTRPNNNTRKSIRIGPGQAFYATGDIIGDIRQAHCNISGAEWN
KTLQQVAAKLREHFNNKTIIFKPSSGGDLEITTHSFNCGGEFFYCNTSGLFNSTWNGTNETITLPCRIKQIVNMWQRVGQAM
YAPPIAGNITCKSNITGLLLTRDGGTNNTETFRPGGGDMRDNWRSELYKYKVVKIEPLGVAPTKAKRRVVEREKRAVGIGAV
FLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLRAIEAQQHLLQLTVWGIKQLQARVLAVERYLKDQQLLGIWGCSG
KLICTTNVPWNSSWSNKSQDEIWDNMTWMQWEREISNYTDIIYSLIEESQNQQEKNEQDLLALDKWASLWNWFDITNWLWYI
KIFIMIVGGLIGLRIVFAVLSIVNRVRQGYSPLSFQTLIPNPRGPDRPGGIEEEGGEQDRDRSIRLVSGFLALAWDDLRSLC

LFSYHRLRDFILIAARTVELLGRRGWEALKYLWNLLQYWGQELKNSAISLLDTTAIAVAEGTDRVIEVVQRACRAILHIPRR
IRQGFERALL$

B **2003 M. Group.anc Env.seq.opt**

ATGCGCGTGATGGGCATCCAGCGCAACTGCCAGCACCTGTGGCGCTGGGGCATCCTGATCTTCGGCATGCTGATGATCTGCT
CCGCCGCCGAGAACCTGTGGGTGACCGTGTACTACGGCGTGCCCGTGTGGAAGGAGGCCAACACCACCCTGTTCTGCGCCTC
CGACGCCAAGGCCTACGACACCGAGGTGCACAACGTGTGGGCCACCCACGCCTGCGTGCCCACCGACCCCAACCCCCAGGAG
ATCGTGCTGGAGAACGTGACCGAGAACTTCAACATGTGGAAGAACAACATGGTGGAGCAGATGCACGAGGACATCATCTCCC
TGTGGGACCAGTCCCTGAAGCCCTGCGTGAAGCTGACCCCCCTGTGCGTGACCCTGAACTGCACCGACGTGAACGCCACCAA
CAACTCCACCAACATGGGCGAGATCAAGAACTGCTCCTTCAACATCACCACCGAGATCCGCGACAAGAAGCAGAAGGTGTAC
GCCCTGTTCTACCGCCTGGACGTGGTGCCCATCAACGACAACAACTCCTACCGCCTGATCAACTGCAACACCTCCGCCATCA
CCCAGGCCTGCCCCAAGGTGTCCTTCGAGCCCATCCCCATCCACTACTGCGCCCCCGCCGGCTTCGCCATCCTGAAGTGCAA
CGACAAGAAGTTCAACGGCACCGGCCCCTGCAAGAACGTGTCCACCGTGCAGTGCACCCACGGCATCAAGCCCGTGGTGTCC
ACCCAGCTGCTGCTGAACGGCTCCCTGGCCGAGGAGGAGATCATCATCCGCTCCGAGAACATCACCGACAACGCCAAGACCA
TCATCGTGCAGCTGAACGAGTCCGTGGAGATCAACTGCACCCGCCCCAACAACAACACCCGCAAGTCCATCCGCATCGGCCC
CGGCCAGGCCTTCTACGCCACCGGCGACATCATCGGCGACATCCGCCAGGCCCACTGCAACATCTCCGGCGCCGAGTGGAAC
AAGACCCTGCAGCAGGTGGCCGCCAAGCTGCGCGAGCACTTCAACAACAAGACCATCATCTTCAAGCCCTCCTCCGGCGGCG
ACCTGGAGATCACCACCCACTCCTTCAACTGCGGCGGCGAGTTCTTCTACTGCAACACCTCCGGCCTGTTCAACTCCACCTG
GAACGGCACCAACGAGACCATCACCCTGCCCTGCCGCATCAAGCAGATCGTGAACATGTGGCAGCGCGTGGGCCAGGCCATG
TACGCCCCCCCCCATCGCCGGCAACATCACCTGCAAGTCCAACATCACCGGCCTGCTGCTGACCCGCGACGGCGGCACCAACA
ACACCGAGACCTTCCGCCCCGGCGGCGGCGACATGCGCGACAACTGGCGCTCCGAGCTGTACAAGTACAAGGTGGTGAAGAT
CGAGCCCCTGGGCGTGGCCCCCACCAAGGCCAAGCGCCGCGTGGTGGAGCGCGAGAAGCGCGCCGTGGGCATCGGCGCCGTG
TTCCTGGGCTTCCTGGGCGCCGCCGGCTCCACCATGGGCGCCGCCTCCATCACCCTGACCGTGCAGGCCCGCCAGCTGCTGT
CCGGCATCGTGCAGCAGCAGTCCAACCTGCTGCGCGCCATCGAGGCCCAGCAGCACCTGCTGCAGCTGACCGTGTGGGGCAT
CAAGCAGCTGCAGGCCCGCGTGCTGGCCGTGGAGCGCTACCTGAAGGACCAGCAGCTGCTGGGCATCTGGGGCTGCTCCGGC
AAGCTGATCTGCACCACCAACGTGCCCTGGAACTCCTCCTGGTCCAACAAGTCCCAGGACGAGATCTGGGACAACATGACCT
GGATGCAGTGGGAGCGCGAGATCTCCAACTACACCGACATCATCTACTCCCTGATCGAGGAGTCCCAGAACCAGCAGGAGAA
GAACGAGCAGGACCTGCTGGCCCTGGACAAGTGGGCCTCCCTGTGGAACTGGTTCGACATCACCAACTGGCTGTGGTACATC
AAGATCTTCATCATGATCGTGGGCGGCCTGATCGGCCTGCGCATCGTGTTCGCCGTGCTGTCCATCGTGAACCGCGTGCGCC
AGGGCTACTCCCCCCTGTCCTTCCAGACCCTGATCCCCAACCCCCGCGGCCCCGACCGCCCCGGCGGCATCGAGGAGGAGGG
CGGCGAGCAGGACCGCGACCGCTCCATCCGCCTGGTGTCCGGCTTCCTGGCCCTGGCCTGGGACGACCTGCGCTCCCTGTGC
CTGTTCTCCTACCACCGCCTGCGCGACTTCATCCTGATCGCCGCCCGCACCGTGGAGCTGCTGGGCCGCCGCGGCTGGGAGG
CCCTGAAGTACCTGTGGAACCTGCTGCAGTACTGGGGCCAGGAGCTGAAGAACTCCGCCATCTCCCTGCTGGACACCACCGC
CATCGCCGTGGCCGAGGGCACCGACCGCGTGATCGAGGTGGTGCAGCGCGCCTGCCGCGCCATCCTGCACATCCCCCGCCGC
ATCCGCCAGGGCTTCGAGCGCGCCCTGCTGTAA

Fig. 41

A **2003 CON_A1 Env**

MRVMGIQRNCQHLLRWGTMILGMIIICSAAENLWVTVYYGVPVWKDAETTLFCASDAKAYETEMHNVWATHACVPTDPNPQE
IHLENVTEEFNMWKNNMVEQMHTDIISLWDQSLKPCVKLTPLCVTLNCSNVNVTNNTTNTHEEEIKNCSFNMTTELRDKKQK
VYSLFYRLDVVQINENNSNSSYRLINCNTSAITQACPKVSFEPIPIHYCAPAGFAILKCKDKEFNGTGPCKNVSTVQCTHGI
KPVVSTQLLLNGSLAEEEVIIRSENITNNAKTIIVQLTKPVKINCTRPNNNTRKSIRIGPGQAFYATGDIIGDIRQAHCNVS
RSEWNKTLQKVAKQLRKYFKNKTIIFTNSSGGDLEITTHSFNCGGEFFYCNTSGLFNSTWNNGTMKNTITLPCRIKQIINMW
QRAGQAMYAPPIQGVIRCESNITGLLLTRDGGNNNTNETFRPGGGDMRDNWRSELYKYKVVKIEPLGVAPTRAKRRVVEREK
RAVGIGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLRAIEAQQHLLKLTVWGIKQLQARVLAVERYLKDQQL
LGIWGCSGKLICTTNVPWNSSWSNKSQNEIWDNMTWLQWDKEISNYTHIIYNLIEESQNQQEKNEQDLLALDKWANLWNWFD
ISNWLWYIKIFIMIVGGLIGLRIVFAVLSVINRVRQGYSPLSFQTHTPNPRGLDRPGRIEEEGGEQGRDRSIRLVSGFLALA
WDDLRSLCLFSYHRLRDFILIAARTVELLGHSSLKGLRLGWEGLKYLWNLLLYWGRELKISAINLVDTIAIAVAGWTDRVIE
IGQRIGRAILHIPRRIRQGLERALL$

B **2003 CON_A1 Env.seq.opt**

ATGCGCGTGATGGGCATCCAGCGCAACTGCCAGCACCTGCTGCGCTGGGGCACCATGATCCTGGGCATGATCATCATCTGCT
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CGACGCCAAGGCCTACGAGACCGAGATGCACAACGTGTGGGCCACCCACGCCTGCGTGCCCACCGACCCCAACCCCCAGGAG
ATCCACCTGGAGAACGTGACCGAGGAGTTCAACATGTGGAAGAACAACATGGTGGAGCAGATGCACACCGACATCATCTCCC
TGTGGGACCAGTCCCTGAAGCCCTGCGTGAAGCTGACCCCCCTGTGCGTGACCCTGAACTGCTCCAACGTGAACGTGACCAA
CAACACCACCAACACCCACGAGGAGGAGATCAAGAACTGCTCCTTCAACATGACCACCGAGCTGCGCGACAAGAAGCAGAAG
GTGTACTCCCTGTTCTACCGCCTGGACGTGGTGCAGATCAACGAGAACAACTCCAACTCCTCCTACCGCCTGATCAACTGCA
ACACCTCCGCCATCACCCAGGCCTGCCCCAAGGTGTCCTTCGAGCCCATCCCCATCCACTACTGCGCCCCCGCCGGCTTCGC
CATCCTGAAGTGCAAGGACAAGGAGTTCAACGGCACCGGCCCCTGCAAGAACGTGTCCACCGTGCAGTGCACCCACGGCATC

AAGCCCGTGGTGTCCACCCAGCTGCTGCTGAACGGCTCCCTGGCCGAGGAGGAGGTGATCATCCGCTCCGAGAACATCACCA
ACAACGCCAAGACCATCATCGTGCAGCTGACCAAGCCCGTGAAGATCAACTGCACCCGCCCCAACAACAACACCCGCAAGTC
CATCCGCATCGGCCCCGGCCAGGCCTTCTACGCCACCGGCGACATCATCGGCGACATCCGCCAGGCCCACTGCAACGTGTCC
CGCTCCGAGTGGAACAAGACCCTGCAGAAGGTGGCCAAGCAGCTGCGCAAGTACTTCAAGAACAAGACCATCATCTTCACCA
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CAGCGCGCCGGCCAGGCCATGTACGCCCCCCCCATCCAGGGCGTGATCCGCTGCGAGTCCAACATCACCGGCCTGCTGCTGA
CCCGCGACGGCGGCAACAACAACACCAACGAGACCTTCCGCCCCGGCGGCGGCGACATGCGCGACAACTGGCGCTCCGAGCT
GTACAAGTACAAGGTGGTGAAGATCGAGCCCCTGGGCGTGGCCCCCACCCGCGCCAAGCGCCGCGTGGTGGAGCGCGAGAAG
CGCGCCGTGGGCATCGGCGCCGTGTTCCTGGGCTTCCTGGGCGCCGCCGGCTCCACCATGGGCGCCGCCTCCATCACCCTGA
CCGTGCAGGCCCGCCAGCTGCTGTCCGGCATCGTGCAGCAGCAGTCCAACCTGCTGCGCGCCATCGAGGCCCAGCAGCACCT
GCTGAAGCTGACCGTGTGGGGCATCAAGCAGCTGCAGGCCCGCGTGCTGGCCGTGGAGCGCTACCTGAAGGACCAGCAGCTG
CTGGGCATCTGGGGCTGCTCCGGCAAGCTGATCTGCACCACCAACGTGCCCTGGAACTCCTCCTGGTCCAACAAGTCCCAGA
ACGAGATCTGGGACAACATGACCTGGCTGCAGTGGGACAAGGAGATCTCCAACTACACCCACATCATCTACAACCTGATCGA
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9.42

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2003 A1.AnC Env

MRVMGIQRNCQHLWRWGTMIFGMIIICSAAENLWVTVYYGVPVWKDAETTLFCASDAKAYDTEVHNVWATHACVPTDPNPQE
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VYSLFYRLDVVPINENNSNSSYRLINCNTSAITQACPKVSFEPIPIHYCAPAGFAILKCKDKEFNGTGPCKNVSTVQCTHGI
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QRVGQAMYAPPIQGVIRCESNITGLLLTRDGGNNNTNETFRPGGGDMRDNWRSELYKYKVVKIEPLGVAPTRAKRRVVEREK
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2003 A1.anc Env.seq.opt

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CCGCCGCCGAGAACCTGTGGGTGACCGTGTACTACGGCGTGCCCGTGTGGAAGGACGCCGAGACCACCCTGTTCTGCGCCTC
CGACGCCAAGGCCTACGACACCGAGGTGCACAACGTGTGGGCCACCCACGCCTGCGTGCCCACCGACCCCAACCCCCAGGAG
ATCGACCTGGAGAACGTGACCGAGGAGTTCAACATGTGGAAGAACAACATGGTGGAGCAGATGCACGCCGACATCATCTCCC
TGTGGGACCAGTCCCTGAAGCCCTGCGTGAAGCTGACCCCCCTGTGCGTGACCCTGAACTGCTCCAACGTGAACGTGACCAA
CAACACCACCAACACCCACGAGGAGGAGATCAAGAACTGCTCCTTCAACATGACCACCGAGCTGCGCGACAAGAAGCAGAAG
GTGTACTCCCTGTTCTACCGCCTGGACGTGGTGCCCATCAACGAGAACAACTCCAACTCCTCCTACCGCCTGATCAACTGCA
ACACCTCCGCCATCACCCAGGCCTGCCCCAAGGTGTCCTTCGAGCCCATCCCCATCCACTACTGCGCCCCCCGCCGGCTTCGC
CATCCTGAAGTGCAAGGACAAGGAGTTCAACGGCACCGGCCCCTGCAAGAACGTGTCCACCGTGCAGTGCACCCACGGCATC
AAGCCCGTGGTGTCCACCCAGCTGCTGCTGAACGGCTCCCTGGCCGAGGAGGAGGTGATGATCCGCTCCGAGAACATCACCG
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CGCACCGAGTGGAACAAGACCCTGCAGAAGGTGGCCGCCCAGCTGCGCAAGCACTTCAACAACAAGACCATCATCTTCAACT
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CCCGCGACGGCGGCAACAACAACACCAACGAGACCTTCCGCCCCGGCGGCGGCGACATGCGCGACAACTGGCGCTCCGAGCT
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CGCGCCGTGGGCCTGGGCGCCGTGTTCCTGGGCTTCCTGGGCGCCGCCGGCTCCACCATGGGCGCCGCCTCCATCACCCTGA
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19.43

2003 CON_A2 Env

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MRVMGTQRNYQHLWRWGILILGMLIMCKATDLWVTVYYGVPVWKDADTTLFCASDAKAYDTEVHNVWATHACVPTDPNPQEV
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NATLQKVAEQLREHFPNKTIIFTNSSGGDLEITTHSFNCGGEFFYCNTTGLFNSTWKNGTTNNTEQMITLPCRIKQIINMWQ
RVGRAMYAPPIAGVIKCTSNITGIILTRDGGNNETETFRPGGGDMRDNWRSELYKYKVVKIEPLGVAPTRAKRRVVEREKRA
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IWGCSGKLICATTVPWNSSWSNKTQEEIWNNMTWLQWDKEISNYTNIIYKLLEESQNQQEKNEQDLLALDKWANLWNWFNIT
NWLWYIRIFIMIVGGLIGLRIVIAIISVVNRVRQGYSPLSFQIPTPNPEGLDRPGRIEEGGGEQGRDRSIRLVSGFLALAWD
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2003 CON_A2 Env.seq.opt

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CGCCAAGGCCTACGACACCGAGGTGCACAACGTGTGGGCCACCCACGCCTGCGTGCCCACCGACCCCAACCCCCAGGAGGTG
AACCTGGAGAACGTGACCGAGGACTTCAACATGTGGAAGAACAACATGGTGGAGCAGATGCACGAGGACATCATCTCCCTGT
GGGACCAGTCCCTGAAGCCCTGCGTGAAGCTGACCCCCCTGTGCGTGACCCTGAACTGCTCCAACGCCAACACCACCAACAA
CTCCACCATGGAGGAGATCAAGAACTGCTCCTACAACATCACCACCGAGCTGCGCGACAAGACCCAGAAGGTGTACTCCCTG
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CCATCACCCAGGCCTGCCCCAAGGTGTCCTTCGAGCCCATCCCCATCCACTACTGCGCCCCCGCCGGCTTCGCCATCCTGAA
GTGCAAGGACCCCCGCTTCAACGGCACCGGCTCCTGCAACAACGTGTCCTCCGTGCAGTGCACCCACGGCATCAAGCCCGTG
GCCTCCACCCAGCTGCTGCTGAACGGCTCCCTGGCCGAGGGCAAGGTGATGATCCGCTCCGAGAACATCACCAACAACGCCA
AGAACATCATCGTGCAGTTCAACAAGCCCGTGCCCATCACCTGCATCCGCCCCAACAACAACACCCGCAAGTCCATCCGCTT
CGGCCCCGGCCAGGCCTTCTACACCAACGACATCATCGGCGACATCCGCCAGGCCCACTGCAACATCAACAAGACCAAGTGG
AACGCCACCCTGCAGAAGGTGGCCGAGCAGCTGCGCGAGCACTTCCCCAACAAGACCATCATCTTCACCAACTCCTCCGGCG
GCGACCTGGAGATCACCACCCACTCCTTCAACTGCGGCGGCGAGTTCTTCTACTGCAACACCACCGGCCTGTTCAACTCCAC
CTGGAAGAACGGCACCACCAACAACACCGAGCAGATGATCACCCTGCCCTGCCGCATCAAGCAGATCATCAACATGTGGCAG
CGCGTGGGCCGCGCCATGTACGCCCCCCCCATCGCCGGCGTGATCAAGTGCACCTCCAACATCACCGGCATCATCCTGACCC
GCGACGGCGGCAACAACGAGACCGAGACCTTCCGCCCCGGCGGCGGCGACATGCGCGACAACTGGCGCTCCGAGCTGTACAA
GTACAAGGTGGTGAAGATCGAGCCCCTGGGCGTGGCCCCCACCCGCGCCAAGCGCCGCGTGGTGGAGCGCGAGAAGCGCGCC
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GCCACTCCTCCCTGAAGGGCCTGCGCCTGGGCTGGGAGGGCCTGAAGTACCTGTGGAACCTGCTGCTGTACTGGGGCCGCGA
GCTGAAGAACTCCGCCATCTCCCTGCTGGACACCATCGCCGTGGCCGTGGCCGAGTGGACCGACCGCGTGATCGAGATCGGC
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18.44

2003 CON_B Env

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MRVKGIRKNYQHLWRWGTMLLGMLMICSAAEKLWVTVYYGVPVWKEATTTLFCASDAKAYDTEVHNVWATHACVPTDPNPQE
VVLENVTENFNMWKNNMVEQMHEDIISLWDQSLKPCVKLTPLCVTLNCTDLMNATNTNTTIIYRWRGEIKNCSFNITTSIRD

KVQKEYALFYKLDVVPIDNDNTSYRLISCNTSVITQACPKVSFEPIPIHYCAPAGFAILKCNDKKFNGTGPCTNVSTVQCTH
GIRPVVSTQLLLNGSLAEEEVVIRSENFTDNAKTIIVQLNESVEINCTRPNNNTRKSIHIGPGRAFYTTGEIIGDIRQAHCN
ISRAKWNNTLKQIVKKLREQFGNKTIVFNQSSGGDPEIVMHSFNCGGEFFYCNTTQLFNSTWNGTWNNTEGNITLPCRIKQI
INMWQEVGKAMYAPPIRGQIRCSSNITGLLLTRDGGNNETEIFRPGGGDMRDNWRSELYKYKVVKIEPLGVAPTKAKRRVVQ
REKRAVGIGAMFLGFLGAAGSTMGAASMTLTVQARQLLSGIVQQQNNLLRAIEAQQHLLQLTVWGIKQLQARVLAVERYLKD
QQLLGIWGCSGKLICTTAVPWNASWSNKSLDEIWDNMTWMEWEREIDNYTSLIYTLIEESQNQQEKNEQELLELDKWASLWN
WFDITNWLWYIKIFIMIVGGLVGLRIVFAVLSIVNRVRQGYSPLSFQTRLPAPRGPDRPEGIEEEGGERDRDRSGRLVDGFL
ALIWDDLRSLCLFSYHRLRDLLLIVTRIVELLGRRGWEVLKYWWNLLQYWSQELKNSAVSLLNATAIAVAEGTDRVIEVVQR
ACRAILHIPRRIRQGLERALL$

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2003 CON_B Env.seq.opt

ATGCGCGTGAAGGGCATCCGCAAGAACTACCAGCACCTGTGGCGCTGGGGCACCATGCTGCTGGGCATGCTGATGATCTGCT
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CGACGCCAAGGCCTACGACACCGAGGTGCACAACGTGTGGGCCACCCACGCCTGCGTGCCCACCGACCCCAACCCCCAGGAG
GTGGTGCTGGAGAACGTGACCGAGAACTTCAACATGTGGAAGAACAACATGGTGGAGCAGATGCACGAGGACATCATCTCCC
TGTGGGACCAGTCCCTGAAGCCCTGCGTGAAGCTGACCCCCCTGTGCGTGACCCTGAACTGCACCGACCTGATGAACGCCAC
CAACACCAACACCACCATCATCTACCGCTGGCGCGGCGAGATCAAGAACTGCTCCTTCAACATCACCACCTCCATCCGCGAC
AAGGTGCAGAAGGAGTACGCCCTGTTCTACAAGCTGGACGTGGTGCCCATCGACAACGACAACACCTCCTACCGCCTGATCT
CCTGCAACACCTCCGTGATCACCCAGGCCTGCCCCAAGGTGTCCTTCGAGCCCATCCCCATCCACTACTGCGCCCCCGCCGG
CTTCGCCATCCTGAAGTGCAACGACAAGAAGTTCAACGGCACCGGCCCCTGCACCAACGTGTCCACCGTGCAGTGCACCCAC
GGCATCCGCCCCGTGGTGTCCACCCAGCTGCTGCTGAACGGCTCCCTGGCCGAGGAGGAGGTGGTGATCCGCTCCGAGAACT
TCACCGACAACGCCAAGACCATCATCGTGCAGCTGAACGAGTCCGTGGAGATCAACTGCACCCGCCCCAACAACAACACCCG
CAAGTCCATCCACATCGGCCCCGGCCGCGCCTTCTACACCACCGGCGAGATCATCGGCGACATCCGCCAGGCCCACTGCAAC
ATCTCCCGCGCCAAGTGGAACAACACCCTGAAGCAGATCGTGAAGAAGCTGCGCGAGCAGTTCGGCAACAAGACCATCGTGT
TCAACCAGTCCTCCGGCGGCGACCCCGAGATCGTGATGCACTCCTTCAACTGCGGCGGCGAGTTCTTCTACTGCAACACCAC
CCAGCTGTTCAACTCCACCTGGAACGGCACCTGGAACAACACCGAGGGCAACATCACCCTGCCCTGCCGCATCAAGCAGATC
ATCAACATGTGGCAGGAGGTGGGCAAGGCCATGTACGCCCCCCCCATCCGCGGCCAGATCCGCTGCTCCTCCAACATCACCG
GCCTGCTGCTGACCCGCGACGGCGGCAACAACGAGACCGAGATCTTCCGCCCCGGCGGCGGCGACATGCGCGACAACTGGCG
CTCCGAGCTGTACAAGTACAAGGTGGTGAAGATCGAGCCCCTGGGCGTGGCCCCCACCAAGGCCAAGCGCCGCGTGGTGCAG
CGCGAGAAGCGCGCCGTGGGCATCGGCGCCATGTTCCTGGGCTTCCTGGGCGCCGCCGGCTCCACCATGGGCGCCGCCTCCA
TGACCCTGACCGTGCAGGCCCGCCAGCTGCTGTCCGGCATCGTGCAGCAGCAGAACAACCTGCTGCGCGCCATCGAGGCCCA
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CAGCAGCTGCTGGGCATCTGGGGCTGCTCCGGCAAGCTGATCTGCACCACCGCCGTGCCCTGGAACGCCTCCTGGTCCAACA
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CCTGATCGAGGAGTCCCAGAACCAGCAGGAGAAGAACGAGCAGGAGCTGCTGGAGCTGGACAAGTGGGCCTCCCTGTGGAAC
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TCGTGGAGCTGCTGGGCCGCCGCGGCTGGGAGGTGCTGAAGTACTGGTGGAACCTGCTGCAGTACTGGTCCCAGGAGCTGAA
GAACTCCGCCGTGTCCCTGCTGAACGCCACCGCCATCGCCGTGGCCGAGGGCACCGACCGCGTGATCGAGGTGGTGCAGCGC
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Fig. 45

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2003 B.anc Env

MRVKGIRKNCQHLWRWGTMLLGMLMICSAAENLWVTVYYGVPVWKEATTTLFCASDAKAYETEVHNVWATHACVPTDPNPQE
VVLENVTENFNMWKNNMVEQMHEDIISLWDQSLKPCVKLTPLCVTLNCTDLLNATNTNSTNMYRWRGEIKNCSFNITTSIRD
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IRPVVSTQLLLNGSLAEEEVVIRSENFTDNAKTIIVQLNESVEINCTRPNNNTRKSIHIGPGRAFYATGEIIGDIRQAHCNL
SRAKWNNTLKQVVTKLREQFDNKTIVFNPSSGGDPEIVMHSFNCGGEFFYCNTTQLFNSTWNGTWNNTEGNITLPCRIKQII
NMWQEVGKAMYAPPIRGQIRCSSNITGLLLTRDGGNNETEIFRPGGGDMRDNWRSELYKYKVVKIEPLGVAPTKAKRRVVQR
EKRAVGIGAMFLGFLGAAGSTMGAASMTLTVQARQLLSGIVQQQNNLLRAIEAQQHLLQLTVWGIKQLQARVLAVERYLRDQ
QLLGIWGCSGKLICTTTVPWNASWSNKSLDEIWNNMTWMEWEREIDNYTGLIYTLIEESQNQQEKNEQELLELDKWASLWNW
FDITNWLWYIKIFIMIVGGLVGLRIVFAVLSIVNRVRQGYSPLSFQTRLPAPRGPDRPEGIEEEGGERDRDRSGRLVNGFLA
LIWDDLRSLCLFSYHRLRDLLLIVARIVELLGRRGWEALKYWWNLLQYWSQELKNSAVSLLNATAIAVAEGTDRVIEVVQRA
CRAILHIPRRIRQGLERALL$

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2003 B.anc Env.seq.opt

ATGCGCGTGAAGGGCATCCGCAAGAACTGCCAGCACCTGTGGCGCTGGGGCACCATGCTGCTGGGCATGCTGATGATCTGCT
CCGCCGCCGAGAACCTGTGGGTGACCGTGTACTACGGCGTGCCCGTGTGGAAGGAGGCCACCACCACCCTGTTCTGCGCCTC

CGACGCCAAGGCCTACGAGACCGAGGTGCACAACGTGTGGGCCACCCACGCCTGCGTGCCCACCGACCCCAACCCCCAGGAG
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TGTGGGACCAGTCCCTGAAGCCCTGCGTGAAGCTGACCCCCCTGTGCGTGACCCTGAACTGCACCGACCTGCTGAACGCCAC
CAACACCAACTCCACCAACATGTACCGCTGGCGCGGCGAGATCAAGAACTGCTCCTTCAACATCACCACCTCCATCCGCGAC
AAGATGCAGAAGGAGTACGCCCTGTTCTACAAGCTGGACGTGGTGCCCATCGACAACAACACCTCCTACCGCCTGATCAACT
GCAACACCTCCGTGATCACCCAGGCCTGCCCCAAGGTGTCCTTCGAGCCCATCCCCATCCACTACTGCACCCCCGCCGGCTT
CGCCATCCTGAAGTGCAACGACAAGAAGTTCAACGGCACCGGCCCCTGCAAGAACGTGTCCACCGTGCAGTGCACCCACGGC
ATCCGCCCCGTGGTGTCCACCCAGCTGCTGCTGAACGGCTCCCTGGCCGAGGAGGAGGTGGTGATCCGCTCCGAGAACTTCA
CCGACAACGCCAAGACCATCATCGTGCAGCTGAACGAGTCCGTGGAGATCAACTGCACCCGCCCCAACAACAACACCCGCAA
GTCCATCCACATCGGCCCCGGCCGCGCCTTCTACGCCACCGGCGAGATCATCGGCGACATCCGCCAGGCCCACTGCAACCTG
TCCCGCGCCAAGTGGAACAACACCCTGAAGCAGGTGGTGACCAAGCTGCGCGAGCAGTTCGACAACAAGACCATCGTGTTCA
ACCCCTCCTCCGGCGGCGACCCCGAGATCGTGATGCACTCCTTCAACTGCGGCGGCGAGTTCTTCTACTGCAACACCACCCA
GCTGTTCAACTCCACCTGGAACGGCACCTGGAACAACACCGAGGGCAACATCACCCTGCCCTGCCGCATCAAGCAGATCATC
AACATGTGGCAGGAGGTGGGCAAGGCCATGTACGCCCCCCCCATCCGCGGCCAGATCCGCTGCTCCTCCAACATCACCGGCC
TGCTGCTGACCCGCGACGGCGGCAACAACGAGACCGAGATCTTCCGCCCCGGCGGCGGCGACATGCGCGACAACTGGCGCTC
CGAGCTGTACAAGTACAAGGTGGTGAAGATCGAGCCCCTGGGCGTGGCCCCCACCAAGGCCAAGCGCCGCGTGGTGCAGCGC
GAGAAGCGCGCCGTGGGCATCGGCGCCATGTTCCTGGGCTTCCTGGGCGCCGCCGGCTCCACCATGGGCGCCGCCTCCATGA
CCCTGACCGTGCAGGCCCGCCAGCTGCTGTCCGGCATCGTGCAGCAGCAGAACAACCTGCTGCGCGCCATCGAGGCCCAGCA
GCACCTGCTGCAGCTGACCGTGTGGGGCATCAAGCAGCTGCAGGCCCGCGTGCTGGCCGTGGAGCGCTACCTGCGCGACCAG
CAGCTGCTGGGCATCTGGGGCTGCTCCGGCAAGCTGATCTGCACCACCACCGTGCCCTGGAACGCCTCCTGGTCCAACAAGT
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TGGAGCTGCTGGGCCGCCGCGGCTGGGAGGCCCTGAAGTACTGGTGGAACCTGCTGCAGTACTGGTCCCAGGAGCTGAAGAA
CTCCGCCGTGTCCCTGCTGAACGCCACCGCCATCGCCGTGGCCGAGGGCACCGACCGCGTGATCGAGGTGGTGCAGCGCGCC
TGCCGCGCCATCCTGCACATCCCCCGCCGCATCCGCCAGGGCCTGGAGCGCGCCCTGCTGTAA

Fig. 46

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2003 CON_C Env

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2003 CON_C Env.seq.opt

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19.47

2003 C.anc Env

A

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2003 C.anc Env.seq.opt

B

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8.48A

2003 CON_D Env

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2003 CON_D Env.seq.opt

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8.49A

2003 CON_F1 Env

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TQWNKTLEQVKAKLKSHFPNKTIKFNSSSGGDLEITMHSFNCRGEFFYCNTSGLFNDTGSNGTITLPCRIKQIVNMWQEVGR
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YIKIFIMIVGGLIGLRIVFAVLSIVNRVRKGYSPLSLQTLIPSPREPDRPEGIEEGGGEQGKDRSVRLVNGFLALVWDDLRN
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RRIRQGLERALL$

3 **2003 CON_F1 Env.seq.opt**

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19.50

A **2003 CON_F2 Env**

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RIRQGFERALL$

B **2003 CON_F2 Env.seq.opt**

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AGACCATCATCGTGCAGTTCAACCGCTCCGTGGAGATCAACTGCACCCGCCCCAACAACAACACCCGCAAGTCCATCCGCAT
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GCGACCTGGAGATCACCACCCACTCCTTCAACTGCCGCGGCGAGTTCTTCTACTGCAACACCTCCGACCTGTTCAACAACAC
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TGTCCGGCATCGTGCAGCAGCAGTCCAACCTGCTGAAGGCCATCGAGGCCCAGCAGCACCTGCTGCAGCTGACCGTGTGGGG
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9.51

A

2003 CON_G Env

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WGCSGKLICTTNVPWNTSWSNKSYNEIWDNMTWIEWEREISNYTQQIYSLIEESQNQQEKNEQDLLALDKWASLWNWFDITK
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B

2003 CON_G Env.seq.opt

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9.52A

2003 CON_H Env

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B

2003 CON_H Env.seq.opt

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9.53A

2003 CON_01_AE Env

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2003 CON_01_AE Env.seq.opt

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Fig. 5A

2003 CON_02_AG Env

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2003 CON_02_AG Env.seq.opt

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2003 CON_03_AB Env

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2003 CON_03_AB Env.seq.opt

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GGCCTACTCCAAGGAGGTGCACAACGTGTGGGCCACCTACGCCTGCGTGCCCACCGACCCCTCCCCCCAGGAGATCCCCCTG
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AGTCCCTGAAGCCCTGCGTGAAGCTGACCCCCCTGTGCGTGACCCTGAACTGCACCGACCTGAAGAAGAACGTGACCTCCAC
CAACACCTCCTCCATCAAGATGATGGAGATGAAGAACTGCTCCTTCAACATCACCACCGACCTGCGCGACAAGGTGAAGAAG
GAGTACGCCCTGTTCTACAAGCTGGACGTGGTGCAGATCGACAACGACTCCTACCGCCTGATCTCCTGCAACACCTCCGTGG
TGACCCAGGCCTGCCCCAAGATCTCCTTCGAGCCCATCCCCATCCACTACTGCGCCCCCGCCGGCTTCGCCATCCTGAAGTG
CAACGACAAGAAGTTCAACGGCACCGGCCCCTGCACCAACGTGTCCACCGTGCAGTGCACCCACGGCATCAAGCCCGTGGTG
TCCACCCAGCTGCTGCTGAACGGCTCCCTGGCCGAGGAGGAGGTGGTGATCCGCTCCGTGAACTTCACCGACAACACCAAGA
CCATCATCGTGCAGCTGAAGGAGCCCGTGGAGATCAACTGCACCCGCCCCAACAACAACACCCGCAAGGGCATCCACATCGG

CCCCGGCCGCGCCTTCTACGCCACCGGCGACATCATCGGCGACATCCGCCAGGCCCACTGCAACATCTCCATCACCAAGTGG
AACAACACCCTGAAGCAGATCGTGATCAAGCTGCGCAAGCAGTTCGGCAACAAGACCATCGTGTTCAACCAGTCCTCCGGCG
GCGACCCCGAGATCGTGATGCACTCCTTCAACTGCGGCGGCGAGTTCTTCTACTGCAACACCACCAAGCTGTTCAACTCCAC
CTGGAACGGCACCGAGGAGCTGAACAACACCGAGGGCGACATCGTGACCCTGCCCTGCCGCATCAAGCAGATCATCAACATG
TGGCAGGAGGTGGGCAAGGCCATGTACGCCCCCCCCATCGCCGGCCAGATCCGCTGCTCCTCCAACATCACCGGCCTGCTGC
TGACCCGCGACGGCGGCAACCAGTCCAACGTGACCGAGATCTTCCGCCCCGGCGGCGGCGACATGCGCGACAACTGGCGCTC
CGAGCTGTACAAGTACAAGGTGGTGAAGATCGAGCCCCTGGGCGTGGCCCCCACCAAGGCCAAGCGCCGCGTGGTGCAGCGC
GAGAAGCGCGCCGTGGGCATCGGCGCCGTGTTCCTGGGCTTCCTGGGCGCCGCCGGCTCCACCATGGGCGCCGCCTCCATCA
CCCTGACCGTGCAGGCCCGCCAGCTGCTGTCCGGCATCGTGCAGCAGCAGAACAACCTGCTGCGCGCCATCGAGGCCCAGCA
GCACCTGCTGCAGCTGACCGTGTGGGGCATCAAGCAGCTGCAGGCCCGCGTGCTGGCCGTGGAGCGCTACCTGAAGGACCAG
CAGCTGCTGGGCATCTGGGGCTGCTCCGGCAAGCTGATCTGCACCACCGCCGTGCCCTGGAACACCTCCTGGTCCAACAAGT
CCCTGGACGAGATCTGGAACAACATGACCTGGATGGAGTGGGAGCGCGAGATCAACAACTACACCGGCCTGATCTACAACCT
GATCGAGGAGTCCCAGAACCAGCAGGAGAAGAACGAGCAGGAGATCCTGGCCCTGGACAAGTGGGCCTCCCTGTGGAACTGG
TTCGACATCTCCAAGTGGCTGTGGTACATCAAGATCTTCATCATGATCGTGGGCGGCCTGGTGGGCCTGCGCATCATCTTCG
CCGTGCTGTCCATCGTGAACCGCGTGCGCCAGGGCTACTCCCCCCTGTCCTTCCAGACCCGCCTGCCCACCCAGCGCGGCCC
CGACCGCCCCGAGGGCATCGAGGAGGAGGGCGGCGAGCGCGACCGCGACACCTCCATCCGCCTGGTGAACGGCTTCCTGGCC
CTGATCTGGGACGACCTGCGCTCCCTGTGCCTGTTCATCTACCACCACCTGCGCGACCTGCTGCTGATCGCCGCCCGCATCG
TGGAGCTGCTGGGCCGCCGCGGCTGGGAGGCCCTGAAGTACTGGTGGAACCTGCTGCAGTACTGGATCCAGGAGCTGAAGTC
CTCCGCCATCAACCTGATCGACACCATCGCCATCGCCGTGGCCGGCTGGACCGACCGCGTGATCGAGATCGGCCAGCGCTTC
TGCCGCGCCATCCGCAACATCCCCCGCCGCATCCGCCAGGGCGCCGAGAAGGCCCTGCAGTAA

1956

2003 CON_04_CPX Env

A

MRVMGIQRNYPHLWEWGTLILGLVIICSASKNLWVTVYYGVPVWRDAETTPFCASDAKAYDKEVHNIWATHACVPTDPNPQE
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EYALFYRLDIVPINDSANNNSINSEYMLINCNASTIKQACPKVTFEPIPIHYCAPAGFAILKCNDKNFTGLGPCTNVSSVQC
THGIKPVVSTQLLLNGSLATEGVVIRSKNFTDNTKNIIVQLAKAVKINCTRPNNNTRKSVHIGPGQTWYATGEIIGDIRQAH
CNISGNDWNETLQKIVEELRKHFPNKTIIFAPSAGGDLEITTHSFNCGGEFFYCNTSELFNSTYMNSTNSTTINKTITLPCR
IKQIVSMWQEVGQAMYAPPIAGSINCSSDITGIILTRDGGNNNTNNETFRPGGGDMRDNWRSELYKYKVVKIEPVGVAPTRA
RRRVVQREKRAVGIGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLRAIEAQQHLLRLTVWGIKQLQARVLAL
ESYLKDQQLLGIWGCSGKLICTTNVPWNSSWSNKSYNDIWDNMTWLQWDKEINNYTQIIYELLEESQNQQEKNEQDLLALDK
WANLWNWFNISNWLWYIKIFIMIVGGLIGLRIIFAVLSIVNRVRQGYSPLSLQTLIPTTQRGPDRPEGTEEEGGEQDRSRSI
RLVNGFLPLIWDDLRNLCLFSYRHLRNLLLIVARTVELLGIRGWEALKYLWNLLLYWGQELRNSAINLLDTTAIAVAEGTDR
IIEAVQRACRAIRNIPRRIRQGLERALL$

2003 CON_04_CPX Env.seq.opt

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CGACGCCAAGGCCTACGACAAGGAGGTGCACAACATCTGGGCCACCCACGCCTGCGTGCCCACCGACCCCAACCCCCAGGAG
ATCGCCCTGAAGAACGTGACCGAGAACTTCAACATGTGGAAGAACAACATGGTGGAGCAGATGCACGAGGACATCATCTCCC
TGTGGGACGAGGGCCTGAAGCCCTGCGTGAAGCTGACCCCCCTGTGCGTGGCCCTGAACTGCTCCAACGCCACCATCAACAA
CTCCACCAAGACCAACTCCACCGAGGAGATCAAGAACTGCTCCTTCAACATCACCACCGAGATCCGCGACAAGAAGAAGAAG
GAGTACGCCCTGTTCTACCGCCTGGACATCGTGCCCATCAACGACTCCGCCAACAACAACTCCATCAACTCCGAGTACATGC
TGATCAACTGCAACGCCTCCACCATCAAGCAGGCCTGCCCCAAGGTGACCTTCGAGCCCATCCCCATCCACTACTGCGCCCC
CGCCGGCTTCGCCATCCTGAAGTGCAACGACAAGAACTTCACCGGCCTGGGCCCCTGCACCAACGTGTCCTCCGTGCAGTGC
ACCCACGGCATCAAGCCCGTGGTGTCCACCCAGCTGCTGCTGAACGGCTCCCTGGCCACCGAGGGCGTGGTGATCCGCTCCA
AGAACTTCACCGACAACACCAAGAACATCATCGTGCAGCTGGCCAAGGCCGTGAAGATCAACTGCACCCGCCCCAACAACAA
CACCCGCAAGTCCGTGCACATCGGCCCCGGCCAGACCTGGTACGCCACCGGCGAGATCATCGGCGACATCCGCCAGGCCCAC
TGCAACATCTCCGGCAACGACTGGAACGAGACCCTGCAGAAGATCGTGGAGGAGCTGCGCAAGCACTTCCCCAACAAGACCA
TCATCTTCGCCCCCTCCGCCGGCGGCGACCTGGAGATCACCACCCACTCCTTCAACTGCGGCGGCGAGTTCTTCTACTGCAA
CACCTCCGAGCTGTTCAACTCCACCTACATGAACTCCACCAACTCCACCACCATCAACAAGACCATCACCCTGCCCTGCCGC
ATCAAGCAGATCGTGTCCATGTGGCAGGAGGTGGGCCAGGCCATGTACGCCCCCCCCATCGCCGGCTCCATCAACTGCTCCT
CCGACATCACCGGCATCATCCTGACCCGCGACGGCGGCAACAACAACACCAACAACGAGACCTTCCGCCCCGGCGGCGGCGA
CATGCGCGACAACTGGCGCTCCGAGCTGTACAAGTACAAGGTGGTGAAGATCGAGCCCGTGGGCGTGGCCCCCACCCGCGCC
CGCCGCCGCGTGGTGCAGCGCGAGAAGCGCGCCGTGGGCATCGGCGCCGTGTTCCTGGGCTTCCTGGGCGCCGCCGGCTCCA
CCATGGGCGCCGCCTCCATCACCCTGACCGTGCAGGCCCGCCAGCTGCTGTCCGGCATCGTGCAGCAGCAGTCCAACCTGCT
GCGCGCCATCGAGGCCCAGCAGCACCTGCTGCGCCTGACCGTGTGGGGCATCAAGCAGCTGCAGGCCCGCGTGCTGGCCCTG
GAGTCCTACCTGAAGGACCAGCAGCTGCTGGGCATCTGGGGCTGCTCCGGCAAGCTGATCTGCACCACCAACGTGCCCTGGA
ACTCCTCCTGGTCCAACAAGTCCTACAACGACATCTGGGACAACATGACCTGGCTGCAGTGGGACAAGGAGATCAACAACTA

CACCCAGATCATCTACGAGCTGCTGGAGGAGTCCCAGAACCAGCAGGAGAAGAACGAGCAGGACCTGCTGGCCCTGGACAAG
TGGGCCAACCTGTGGAACTGGTTCAACATCTCCAACTGGCTGTGGTACATCAAGATCTTCATCATGATCGTGGGCGGCCTGA
TCGGCCTGCGCATCATCTTCGCCGTGCTGTCCATCGTGAACCGCGTGCGCCAGGGCTACTCCCCCCTGTCCCTGCAGACCCT
GATCCCCACCACCCAGCGCGGCCCCGACCGCCCCGAGGGCACCGAGGAGGAGGGCGGCGAGCAGGACCGCTCCCGCTCCATC
CGCCTGGTGAACGGCTTCCTGCCCCTGATCTGGGACGACCTGCGCAACCTGTGCCTGTTCTCCTACCGCCACCTGCGCAACC
TGCTGCTGATCGTGGCCCGCACCGTGGAGCTGCTGGGCATCCGCGGCTGGGAGGCCCTGAAGTACCTGTGGAACCTGCTGCT
GTACTGGGGCCAGGAGCTGCGCAACTCCGCCATCAACCTGCTGGACACCACCGCCATCGCCGTGGCCGAGGGCACCGACCGC
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TGTAA

9.57

2003 CON_06_CPX Env

A

MRVKGIQKNWQHLWKWGTLILGLVIICSASNNMWVTVYYGVPAWEDADTILFCASDAKAYSAEKHNVWATHACVPTDPNPQE
IALENVTENFNMWKNHMVEQMHEDIISLWDESLKPCVKLTPLCVTLNCTNVTKNNNTKIMGREEIKNCSFNVTTEIRDKKKK
EYALFYRLDVVPIDDNNNSYRLINCNASTIKQACPKVSFEPIPIHYCAPAGFAILKCRDKNFNGTGPCKNVSTVQCTHGIKP
VVSTQLLLNGSLAEEEIIIKSENLTDNTKTIIVQLNKSVEIRCTRPNNNTRKSISFGPGQAFYATGDIIGDIRQAHCNVSRT
DWNNMLQNVTAKLKELFNKNITFNSSAGGDLEITTHSFNCGGEFFYCNTSQLFNSTRPNETNTITLPCKIKQIVRMWQRVGQ
AMYAPPIAGNITCTSNITGLLLTRDGNNNDSETFRPGGGDMRDNWRSELYKYKVVKIKPLGIAPTRARRRVVGREKRAVGLG
AVFLGFLGTAGSTMGAASITLTVQVRQLLSGIVQQQSNLLRAIEAQQHLLQLTVWGIKQLQARVLAVERYLKDQQLLGIWGC
SGKLICPTNVPWNASWSNKTYNEIWDNMTWIEWDREINNYTQQIYSLIEESQNQQEKNEQDLLALDKWASLWSWFDISNWLW
YIKIFIMIVGGLIGLRIVFAVLSIVNRVRQGYSPLSLQTLIPNPTGADRPGEIEEGGGEQGRTRSIRLVNGFLALAWDDLRS
LCLFSYHRLRDFVLIAARTVETLGHRGWEILKYLGNLVCYWGQELKNSAISLLDTTAIAVANWTDRVIEVVQRVFRAFLNIP
RRIRQGFERALL$

2003 CON_06_CPX Env.seq.opt

B

ATGCGCGTGAAGGGCATCCAGAAGAACTGGCAGCACCTGTGGAAGTGGGGCACCCTGATCCTGGGCCTGGTGATCATCTGCT
CCGCCTCCAACAACATGTGGGTGACCGTGTACTACGGCGTGCCCGCCTGGGAGGACGCCGACACCATCCTGTTCTGCGCCTC
CGACGCCAAGGCCTACTCCGCCGAGAAGCACAACGTGTGGGCCACCCACGCCTGCGTGCCCACCGACCCCAACCCCCAGGAG
ATCGCCCTGGAGAACGTGACCGAGAACTTCAACATGTGGAAGAACCACATGGTGGAGCAGATGCACGAGGACATCATCTCCC
TGTGGGACGAGTCCCTGAAGCCCTGCGTGAAGCTGACCCCCCTGTGCGTGACCCTGAACTGCACCAACGTGACCAAGAACAA
CAACACCAAGATCATGGGCCGCGAGGAGATCAAGAACTGCTCCTTCAACGTGACCACCGAGATCCGCGACAAGAAGAAGAAG
GAGTACGCCCTGTTCTACCGCCTGGACGTGGTGCCCATCGACGACAACAACAACTCCTACCGCCTGATCAACTGCAACGCCT
CCACCATCAAGCAGGCCTGCCCCAAGGTGTCCTTCGAGCCCATCCCCATCCACTACTGCGCCCCCGCCGGCTTCGCCATCCT
GAAGTGCCGCGACAAGAACTTCAACGGCACCGGCCCCTGCAAGAACGTGTCCACCGTGCAGTGCACCCACGGCATCAAGCCC
GTGGTGTCCACCCAGCTGCTGCTGAACGGCTCCCTGGCCGAGGAGGAGATCATCATCAAGTCCGAGAACCTGACCGACAACA
CCAAGACCATCATCGTGCAGCTGAACAAGTCCGTGGAGATCCGCTGCACCCGCCCCAACAACAACACCCGCAAGTCCATCTC
CTTCGGCCCCGGCCAGGCCTTCTACGCCACCGGCGACATCATCGGCGACATCCGCCAGGCCCACTGCAACGTGTCCCGCACC
GACTGGAACAACATGCTGCAGAACGTGACCGCCAAGCTGAAGGAGCTGTTCAACAAGAACATCACCTTCAACTCCTCCGCCG
GCGGCGACCTGGAGATCACCACCCACTCCTTCAACTGCGGCGGCGAGTTCTTCTACTGCAACACCTCCCAGCTGTTCAACTC
CACCCGCCCCAACGAGACCAACACCATCACCCTGCCCTGCAAGATCAAGCAGATCGTGCGCATGTGGCAGCGCGTGGGCCAG
GCCATGTACGCCCCCCCCATCGCCGGCAACATCACCTGCACCTCCAACATCACCGGCCTGCTGCTGACCCGCGACGGCAACA
ACAACGACTCCGAGACCTTCCGCCCCGGCGGCGGCGACATGCGCGACAACTGGCGCTCCGAGCTGTACAAGTACAAGGTGGT
GAAGATCAAGCCCCTGGGCATCGCCCCCACCCGCGCCCGCCGCCGCGTGGTGGGCCGCGAGAAGCGCGCCGTGGGCCTGGGC
GCCGTGTTCCTGGGCTTCCTGGGCACCGCCGGCTCCACCATGGGCGCCGCCTCCATCACCCTGACCGTGCAGGTGCGCCAGC
TGCTGTCCGGCATCGTGCAGCAGCAGTCCAACCTGCTGCGCGCCATCGAGGCCCAGCAGCACCTGCTGCAGCTGACCGTGTG
GGGCATCAAGCAGCTGCAGGCCCGCGTGCTGGCCGTGGAGCGCTACCTGAAGGACCAGCAGCTGCTGGGCATCTGGGGCTGC
TCCGGCAAGCTGATCTGCCCCACCAACGTGCCCTGGAACGCCTCCTGGTCCAACAAGACCTACAACGAGATCTGGGACAACA
TGACCTGGATCGAGTGGGACCGCGAGATCAACAACTACACCCAGCAGATCTACTCCCTGATCGAGGAGTCCCAGAACCAGCA
GGAGAAGAACGAGCAGGACCTGCTGGCCCTGGACAAGTGGGCCTCCCTGTGGTCCTGGTTCGACATCTCCAACTGGCTGTGG
TACATCAAGATCTTCATCATGATCGTGGGCGGCCTGATCGGCCTGCGCATCGTGTTCGCCGTGCTGTCCATCGTGAACCGCG
TGCGCCAGGGCTACTCCCCCCTGTCCCTGCAGACCCTGATCCCCAACCCCACCGGCGCCGACCGCCCCGGCGAGATCGAGGA
GGGCGGCGGCGAGCAGGGCCGCACCCGCTCCATCCGCCTGGTGAACGGCTTCCTGGCCCTGGCCTGGGACGACCTGCGCTCC
CTGTGCCTGTTCTCCTACCACCGCCTGCGCGACTTCGTGCTGATCGCCGCCCGCACCGTGGAGACCCTGGGCCACCGCGGCT
GGGAGATCCTGAAGTACCTGGGCAACCTGGTGTGCTACTGGGGCCAGGAGCTGAAGAACTCCGCCATCTCCCTGCTGGACAC
CACCGCCATCGCCGTGGCCAACTGGACCGACCGCGTGATCGAGGTGGTGCAGCGCGTGTTCCGCGCCTTCCTGAACATCCCC
CGCCGCATCCGCCAGGGCTTCGAGCGCGCCCTGCTGTAA

Fig. 58

A

2003 CON_08_BC Env

MRVRGTRRNYQQWWIWGVLGFWMLMICNVEGNLWVTVYYGVPVWKEAKTTLFCASDAKAYETEVHNVWATHACVPTDPNPQE
IVMENVTENFNMWNNDMVNQMHEDVISLWDQSLKPCVKLTPLCVTLECTNVSSNGNGTYNETYNESVKEIKNCSFNATTLLR
DRKKTVYALFYRLDIVPLNDENSGKNSSEYYRLINCNTSAITQACPKVTFDPIPIHYCTPAGYAILKCNDKKFNGTGQCHNV
STVQCTHGIKPVVSTQLLLNGSLAEREIIIRSENLTNNVKTIIVHLNQSVEIVCTRPNNNTRKSIRIGPGQTFYATGDIIGD
IRQAHCNISKDKWYETLQRVSKKLAEHFPNKTIKFASSSGGDLEITTHSFNCRGEFFYCNTSGLFNGTYMNGTNNSSSIITI
PCRIKQIINMWQEVGRAMYAPPIEGNITCKSNITGLLLVRDGGRTESNNTEIFRPGGGDMRNNWRNELYKYKVVEIKPLGVA
PTAAKRRVVEREKRAVGLGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLRAIEAQQHMLQLTVWGIKQLQTR
VLAIERYLKDQQLLGIWGCSGKLICTTAVPWNSSWSNKSQQEIWDNMTWMQWDKEISNYTNTIYRLLEDSQNQQERNEKDLL
ALDSWKNLWSWFDITNWLWYIKIFIMIVGGLIGLRIIFAVLSIVNRVRQGYSPLSFQILTPNPGGPGRLGRIEEEGGEQDKT
RSIRLVNGFLALAWDDLRNLCLFSYHRLRDFILLTARGVELLGRNSLRGLQRGWEALKYLGSLVQYWGLELKKSTISLVDTI
AIAVAEGTDRIINIVQGICRAIHNIPRRIRQGFEAALQ$

B

2003 CON_08_BC Env seq.opt

ATGCGCGTGCGCGGCACCCGCCGCAACTACCAGCAGTGGTGGATCTGGGGCGTGCTGGGCTTCTGGATGCTGATGATCTGCA
ACGTGGAGGGCAACCTGTGGGTGACCGTGTACTACGGCGTGCCCGTGTGGAAGGAGGCCAAGACCACCCTGTTCTGCGCCTC
CGACGCCAAGGCCTACGAGACCGAGGTGCACAACGTGTGGGCCACCCACGCCTGCGTGCCCACCGACCCCAACCCCCAGGAG
ATCGTGATGGAGAACGTGACCGAGAACTTCAACATGTGGAACAACGACATGGTGAACCAGATGCACGAGGACGTGATCTCCC
TGTGGGACCAGTCCCTGAAGCCCTGCGTGAAGCTGACCCCCCTGTGCGTGACCCTGGAGTGCACCAACGTGTCCTCCAACGG
CAACGGCACCTACAACGAGACCTACAACGAGTCCGTGAAGGAGATCAAGAACTGCTCCTTCAACGCCACCACCCTGCTGCGC
GACCGCAAGAAGACCGTGTACGCCCTGTTCTACCGCCTGGACATCGTGCCCCTGAACGACGAGAACTCCGGCAAGAACTCCT
CCGAGTACTACCGCCTGATCAACTGCAACACCTCCGCCATCACCCAGGCCTGCCCCAAGGTGACCTTCGACCCCATCCCCAT
CCACTACTGCACCCCCGCCGGCTACGCCATCCTGAAGTGCAACGACAAGAAGTTCAACGGCACCGGCCAGTGCCACAACGTG
TCCACCGTGCAGTGCACCCACGGCATCAAGCCCGTGGTGTCCACCCAGCTGCTGCTGAACGGCTCCCTGGCCGAGCGCGAGA
TCATCATCCGCTCCGAGAACCTGACCAACAACGTGAAGACCATCATCGTGCACCTGAACCAGTCCGTGGAGATCGTGTGCAC
CCGCCCCAACAACAACACCCGCAAGTCCATCCGCATCGGCCCCGGCCAGACCTTCTACGCCACCGGCGACATCATCGGCGAC
ATCCGCCAGGCCCACTGCAACATCTCCAAGGACAAGTGGTACGAGACCCTGCAGCGCGTGTCCAAGAAGCTGGCCGAGCACT
TCCCCAACAAGACCATCAAGTTCGCCTCCTCCTCCGGCGGCGACCTGGAGATCACCACCCACTCCTTCAACTGCCGCGGCGA
GTTCTTCTACTGCAACACCTCCGGCCTGTTCAACGGCACCTACATGAACGGCACCAACAACTCCTCCTCCATCATCACCATC
CCCTGCCGCATCAAGCAGATCATCAACATGTGGCAGGAGGTGGGCCGCGCCATGTACGCCCCCCCCCATCGAGGGCAACATCA
CCTGCAAGTCCAACATCACCGGCCTGCTGCTGGTGCGCGACGGCGGCCGCACCGAGTCCAACAACACCGAGATCTTCCGCCC
CGGCGGCGGCGACATGCGCAACAACTGGCGCAACGAGCTGTACAAGTACAAGGTGGTGGAGATCAAGCCCCTGGGCGTGGCC
CCCACCGCCGCCAAGCGCCGCGTGGTGGAGCGCGAGAAGCGCGCCGTGGGCCTGGGCGCCGTGTTCCTGGGCTTCCTGGGCG
CCGCCGGCTCCACCATGGGCGCCGCCTCCATCACCCTGACCGTGCAGGCCCGCCAGCTGCTGTCCGGCATCGTGCAGCAGCA
GTCCAACCTGCTGCGCGCCATCGAGGCCCAGCAGCACATGCTGCAGCTGACCGTGTGGGGCATCAAGCAGCTGCAGACCCGC
GTGCTGGCCATCGAGCGCTACCTGAAGGACCAGCAGCTGCTGGGCATCTGGGGCTGCTCCGGCAAGCTGATCTGCACCACCG
CCGTGCCCTGGAACTCCTCCTGGTCCAACAAGTCCCAGCAGGAGATCTGGGACAACATGACCTGGATGCAGTGGGACAAGGA
GATCTCCAACTACACCAACACCATCTACCGCCTGCTGGAGGACTCCCAGAACCAGCAGGAGCGCAACGAGAAGGACCTGCTG
GCCCTGGACTCCTGGAAGAACCTGTGGTCCTGGTTCGACATCACCAACTGGCTGTGGTACATCAAGATCTTCATCATGATCG
TGGGCGGCCTGATCGGCCTGCGCATCATCTTCGCCGTGCTGTCCATCGTGAACCGCGTGCGCCAGGGCTACTCCCCCCTGTC
CTTCCAGATCCTGACCCCCAACCCCGGCGGCCCCGGCCGCCTGGGCCGCATCGAGGAGGAGGGCGGCGAGCAGGACAAGACC
CGCTCCATCCGCCTGGTGAACGGCTTCCTGGCCCTGGCCTGGGACGACCTGCGCAACCTGTGCCTGTTCTCCTACCACCGCC
TGCGCGACTTCATCCTGCTGACCGCCCGCGGCGTGGAGCTGCTGGGCCGCAACTCCCTGCGCGGCCTGCAGCGCGGCTGGGA
GGCCCTGAAGTACCTGGGCTCCCTGGTGCAGTACTGGGGCCTGGAGCTGAAGAAGTCCACCATCTCCCTGGTGGACACCATC
GCCATCGCCGTGGCCGAGGGCACCGACCGCATCATCAACATCGTGCAGGGCATCTGCCGCGCCATCCACAACATCCCCCGCC
GCATCCGCCAGGGCTTCGAGGCCGCCCTGCAGTAA

Fig. 59A

2003 CON_10_CD Env

MRVMGIQRNCQQWWIWGILGFWMLMICNATGNLWVTVYYGVPVWKETTTTLFCASDAKAYKAEAHNIWATHACVPTDPNPQE
IVLENVTENFNMWKNGMVDQMHEDIISLWDQGLKPCVKLTPLCVTLNCSDVNATNSATNTVVAGMKNCSFNITTEIRDKKKQ
EYALFYKLDVVQIDGSNTSYRLINCNTSAITQACPKVTFEPIPIHYCAPAGFAILKCNDKKFNGTGPCKNVSTVQCTHGIKP
VVSTQLLLNGSLAEEEIIIRSENLTDNAKTIIVQLNESVTINCTRPNNNTRKSIRIGPGQTFYATGDIIGNIRQAYCNISGT
EWNKTLQQVAKKLGDLLNKTTIIFKPSSGGDPEITTHTFNCGGEFFYCNTSKLFNSSWTSNNTGNTSTITLPCRIKQIINMW
QGVGKAIYAPPIAGLINCSSNITGLLLTRDGGANNSETFRPGGGDMRDNWRSELYKYKVVKIEPLGLAPTKAKRRVVEREKR
AIGLGAVFLGFLGAAGSTMGAASLTLTVQARQLLSGIVQQQNNLLRAIEAQQHLLQLTVWGIKQLQARVLAVESYLKDQQLL
GIWGCSGKHICTTNVPWNSSWSNKSLEEIWDNMTWMEWEREIDNYTGLIYSLIEESQNQQEKNEQELLQLDKWASLWNWFSI
TNWLWYIKIFIMIVGGLIGLRIVFAVLSLVNRVRQGYSPLSFQTLLPAPRGPDRPEGIEEEGGEQGRGRSIRLVNGFSALIW
DDLRNLCLFSYHRLRDLILIATRIVELLGRRGWEAIKYLWNLLQYWIQELKNSAISLLDTTAIAVAEGTDRAIEIVQRAVRA
VLNIPTRIRQGLERALL$

3

2003 CON_10_CD Env.seq.opt

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ACGCCACCGGCAACCTGTGGGTGACCGTGTACTACGGCGTGCCCGTGTGGAAGGAGACCACCACCACCCTGTTCTGCGCCTC
CGACGCCAAGGCCTACAAGGCCGAGGCCCACAACATCTGGGCCACCCACGCCTGCGTGCCCACCGACCCCAACCCCCAGGAG
ATCGTGCTGGAGAACGTGACCGAGAACTTCAACATGTGGAAGAACGGCATGGTGGACCAGATGCACGAGGACATCATCTCCC
TGTGGGACCAGGGCCTGAAGCCCTGCGTGAAGCTGACCCCCCTGTGCGTGACCCTGAACTGCTCCGACGTGAACGCCACCAA
CTCCGCCACCAACACCGTGGTGGCCGGCATGAAGAACTGCTCCTTCAACATCACCACCGAGATCCGCGACAAGAAGAAGCAG
GAGTACGCCCTGTTCTACAAGCTGGACGTGGTGCAGATCGACGGCTCCAACACCTCCTACCGCCTGATCAACTGCAACACCT
CCGCCATCACCCAGGCCTGCCCCAAGGTGACCTTCGAGCCCATCCCCATCCACTACTGCGCCCCCGCCGGCTTCGCCATCCT
GAAGTGCAACGACAAGAAGTTCAACGGCACCGGCCCCTGCAAGAACGTGTCCACCGTGCAGTGCACCCACGGCATCAAGCCC
GTGGTGTCCACCCAGCTGCTGCTGAACGGCTCCCTGGCCGAGGAGGAGATCATCATCCGCTCCGAGAACCTGACCGACAACG
CCAAGACCATCATCGTGCAGCTGAACGAGTCCGTGACCATCAACTGCACCCGCCCCAACAACAACACCCGCAAGTCCATCCG
CATCGGCCCCGGCCAGACCTTCTACGCCACCGGCGACATCATCGGCAACATCCGCCAGGCCTACTGCAACATCTCCGGCACC
GAGTGGAACAAGACCCTGCAGCAGGTGGCCAAGAAGCTGGGCGACCTGCTGAACAAGACCACCATCATCTTCAAGCCCTCCT
CCGGCGGCGACCCCGAGATCACCACCCACACCTTCAACTGCGGCGGCGAGTTCTTCTACTGCAACACCTCCAAGCTGTTCAA
CTCCTCCTGGACCTCCAACAACACCGGCAACACCTCCACCATCACCCTGCCCTGCCGCATCAAGCAGATCATCAACATGTGG
CAGGGCGTGGGCAAGGCCATCTACGCCCCCCCCCATCGCCGGCCTGATCAACTGCTCCTCCAACATCACCGGCCTGCTGCTGA
CCCGCGACGGCGGCGCCAACAACTCCGAGACCTTCCGCCCCGGCGGCGGCGACATGCGCGACAACTGGCGCTCCGAGCTGTA
CAAGTACAAGGTGGTGAAGATCGAGCCCCTGGGCCTGGCCCCCACCAAGGCCAAGCGCCGCGTGGTGGAGCGCGAGAAGCGC
GCCATCGGCCTGGGCGCCGTGTTCCTGGGCTTCCTGGGCGCCGCCGGCTCCACCATGGGCGCCGCCTCCCTGACCCTGACCG
TGCAGGCCCGCCAGCTGCTGTCCGGCATCGTGCAGCAGCAGAACAACCTGCTGCGCGCCATCGAGGCCCAGCAGCACCTGCT
GCAGCTGACCGTGTGGGGCATCAAGCAGCTGCAGGCCCGCGTGCTGGCCGTGGAGTCCTACCTGAAGGACCAGCAGCTGCTG
GGCATCTGGGGCTGCTCCGGCAAGCACATCTGCACCACCAACGTGCCCTGGAACTCCTCCTGGTCCAACAAGTCCCTGGAGG
AGATCTGGGACAACATGACCTGGATGGAGTGGGAGCGCGAGATCGACAACTACACCGGCCTGATCTACTCCCTGATCGAGGA
GTCCCAGAACCAGCAGGAGAAGAACGAGCAGGAGCTGCTGCAGCTGGACAAGTGGGCCTCCCTGTGGAACTGGTTCTCCATC
ACCAACTGGCTGTGGTACATCAAGATCTTCATCATGATCGTGGGCGGCCTGATCGGCCTGCGCATCGTGTTCGCCGTGCTGT
CCCTGGTGAACCGCGTGCGCCAGGGCTACTCCCCCCTGTCCTTCCAGACCCTGCTGCCCGCCCCCCGCGGCCCCGACCGCCC
CGAGGGCATCGAGGAGGAGGGCGGCGAGCAGGGCCGCGGCCGCTCCATCCGCCTGGTGAACGGCTTCTCCGCCCTGATCTGG
GACGACCTGCGCAACCTGTGCCTGTTCTCCTACCACCGCCTGCGCGACCTGATCCTGATCGCCACCCGCATCGTGGAGCTGC
TGGGCCGCCGCGGCTGGGAGGCCATCAAGTACCTGTGGAACCTGCTGCAGTACTGGATCCAGGAGCTGAAGAACTCCGCCAT
CTCCCTGCTGGACACCACCGCCATCGCCGTGGCCGAGGGCACCGACCGCGCCATCGAGATCGTGCAGCGCGCCGTGCGCGCC
GTGCTGAACATCCCCACCCGCATCCGCCAGGGCCTGGAGCGCGCCCTGCTGTAA

Fig. 6A

2003 CON_11_CPX Env

MRVKETQRNWHNLWRWGLMIFGMLMICNATENLWVTVYYGVPVWKDADTTLFCASDAKAYSTEKHNVWATHACVPTDPNPQE
IPLENVTENFNMWKNNMVEQMHEDIISLWDESLKPCVKLTPLCVTLNCTDVKNATNTTVEAAEIKNCSFNITTEIKDKKKKE
YALFYKLDVVPINDNNNSIYRLINCNVSTVKQACPKVTFEPIPIHYCAPAGFAILKCNDKKFNGTGPCKNVSTVQCTHGIKP
VVSTQLLLNGSLAEGEVRIRSENFTNNAKTIIVQLNSSVRINCTRPNNNTRKSIHIGPGQAFYATGDIIGDIRQAHCNISRA
EWNNTLQQVAKQLRENFNKTIIFNNPSGGDLEITTHSFNCGGEFFYCNTSRLFNSTWNNDTRNDTKQMHITLPCRIKQIVNM
WQRVGQAMYAPPIQGKIRCNSNITGLLLTRDGGNNNTNETFRPTGGDMRDNWRSELYKYKVVEIKPLGVAPTRAKRRVVERE
KRAVGIGAVLLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLKAIEAQQHLLKLTVWGIKQLQARVLAVERYLKDQQ
LLGIWGCSGKLICTTNVPWNFSWSNKSYDEIWDNMTWIEWEREINNYTQTIYTLLEESQNQQEKNEQDLLALDKWASLWNWF
DISNWLWYIKIFIMIVGGLIGLRIIFAVLSIVNRCRQGYSPLSFQTLTPNHKEADRPGGIEEGGGEQDRTRSIRLVSGFLAL
AWDDLRNLCLFSYHRLRDFILIAARIVETLGRRGWEILKYLGNLAQYWGQELKNSAISLLNATAIAVAEGTDRIIEVVHRVL
RAILHIPRRIRQGFERALL$

2003 CON_11_CPX Env.seq.opt

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ATGCGCGTGAAGGAGACCCAGCGCAACTGGCACAACCTGTGGCGCTGGGGCCTGATGATCTTCGGCATGCTGATGATCTGCA
ACGCCACCGAGAACCTGTGGGTGACCGTGTACTACGGCGTGCCCGTGTGGAAGGACGCCGACACCACCCTGTTCTGCGCCTC
CGACGCCAAGGCCTACTCCACCGAGAAGCACAACGTGTGGGCCACCCACGCCTGCGTGCCCACCGACCCCAACCCCCAGGAG
ATCCCCCTGGAGAACGTGACCGAGAACTTCAACATGTGGAAGAACAACATGGTGGAGCAGATGCACGAGGACATCATCTCCC
TGTGGGACGAGTCCCTGAAGCCCTGCGTGAAGCTGACCCCCCTGTGCGTGACCCTGAACTGCACCGACGTGAAGAACGCCAC
CAACACCACCGTGGAGGCCGCCGAGATCAAGAACTGCTCCTTCAACATCACCACCGAGATCAAGGACAAGAAGAAGAAGGAG
TACGCCCTGTTCTACAAGCTGGACGTGGTGCCCATCAACGACAACAACAACTCCATCTACCGCCTGATCAACTGCAACGTGT
CCACCGTGAAGCAGGCCTGCCCCAAGGTGACCTTCGAGCCCATCCCCATCCACTACTGCGCCCCCGCCGGCTTCGCCATCCT
GAAGTGCAACGACAAGAAGTTCAACGGCACCGGCCCCTGCAAGAACGTGTCCACCGTGCAGTGCACCCACGGCATCAAGCCC
GTGGTGTCCACCCAGCTGCTGCTGAACGGCTCCCTGGCCGAGGGCGAGGTGCGCATCCGCTCCGAGAACTTCACCAACAACG
CCAAGACCATCATCGTGCAGCTGAACTCCTCCGTGCGCATCAACTGCACCCGCCCCAACAACAACACCCGCAAGTCCATCCA
CATCGGCCCCGGCCAGGCCTTCTACGCCACCGGCGACATCATCGGCGACATCCGCCAGGCCCACTGCAACATCTCCCGCGCC

GAGTGGAACAACACCCTGCAGCAGGTGGCCAAGCAGCTGCGCGAGAACTTCAACAAGACCATCATCTTCAACAACCCCTCCG
GCGGCGACCTGGAGATCACCACCCACTCCTTCAACTGCGGCGGCGAGTTCTTCTACTGCAACACCTCCCGCCTGTTCAACTC
CACCTGGAACAACGACACCCGCAACGACACCAAGCAGATGCACATCACCCTGCCCTGCCGCATCAAGCAGATCGTGAACATG
TGGCAGCGCGTGGGCCAGGCCATGTACGCCCCCCCCATCCAGGGCAAGATCCGCTGCAACTCCAACATCACCGGCCTGCTGC
TGACCCGCGACGGCGGCAACAACAACACCAACGAGACCTTCCGCCCCACCGGCGGCGACATGCGCGACAACTGGCGCTCCGA
GCTGTACAAGTACAAGGTGGTGGAGATCAAGCCCCTGGGCGTGGCCCCCACCCGCGCCAAGCGCCGCGTGGTGGAGCGCGAG
AAGCGCGCCGTGGGCATCGGCGCCGTGCTGCTGGGCTTCCTGGGCGCCGCCGGCTCCACCATGGGCGCCGCCTCCATCACCC
TGACCGTGCAGGCCCGCCAGCTGCTGTCCGGCATCGTGCAGCAGCAGTCCAACCTGCTGAAGGCCATCGAGGCCCAGCAGCA
CCTGCTGAAGCTGACCGTGTGGGGCATCAAGCAGCTGCAGGCCCGCGTGCTGGCCGTGGAGCGCTACCTGAAGGACCAGCAG
CTGCTGGGCATCTGGGGCTGCTCCGGCAAGCTGATCTGCACCACCAACGTGCCCTGGAACTTCTCCTGGTCCAACAAGTCCT
ACGACGAGATCTGGGACAACATGACCTGGATCGAGTGGGAGCGCGAGATCAACAACTACACCCAGACCATCTACACCCTGCT
GGAGGAGTCCCAGAACCAGCAGGAGAAGAACGAGCAGGACCTGCTGGCCCTGGACAAGTGGGCCTCCCTGTGGAACTGGTTC
GACATCTCCAACTGGCTGTGGTACATCAAGATCTTCATCATGATCGTGGGCGGCCTGATCGGCCTGCGCATCATCTTCGCCG
TGCTGTCCATCGTGAACCGCTGCCGCCAGGGCTACTCCCCCCTGTCCTTCCAGACCCTGACCCCCAACCACAAGGAGGCCGA
CCGCCCCGGCGGCATCGAGGAGGGCGGCGGCGAGCAGGACCGCACCCGCTCCATCCGCCTGGTGTCCGGCTTCCTGGCCCTG
GCCTGGGACGACCTGCGCAACCTGTGCCTGTTCTCCTACCACCGCCTGCGCGACTTCATCCTGATCGCCGCCCGCATCGTGG
AGACCCTGGGCCGCCGCGGCTGGGAGATCCTGAAGTACCTGGGCAACCTGGCCCAGTACTGGGGCCAGGAGCTGAAGAACTC
CGCCATCTCCCTGCTGAACGCCACCGCCATCGCCGTGGCCGAGGGCACCGACCGCATCATCGAGGTGGTGCACCGCGTGCTG
CGCGCCATCCTGCACATCCCCCGCCGCATCCGCCAGGGCTTCGAGCGCGCCCTGCTGTAA

9.61

A

2003 CON_12_BF Env

MRVRGMQRNWQHLGKWGLLFLGILIICNATENLWVTVYYGVPVWKEATTTLFCASDAKSYEREVHNVWATHACVPTDPNPQE
VDLENVTENFDMWKNNMVEQMHTDIISLWDQSLKPCVKLTPLCVTLNCTDANATANATKEHPEGRAGAIQNCSFNMTTEVRD
KQMKVQALFYRLDIVPISDNNSNEYRLINCNTSTITQACPKVSWDPIPIHYCAPAGYAILKCNDKKFNGTGPCKNVSTVQCT
HGIKPVVSTQLLLNGSLAEEEIIIRSQNISDNAKTIIVHLNESVQINCTRPNNNTRKSIHIGPGRAFYATGDIIGDIRKAHC
NVSGTQWNKTLEQVKKKLRSYFNTTIKFNSSSGGDPEITMHSFNCRGEFFYCNTSKLFNDTVSNDTIILPCRIKQIVNMWQE
VGRAMYAAPIAGNITCTSNITGLLLTRDGGHNETNKTETFRPGGGNMKDNWRSELYKYKVVEIEPLGVAPTRAKRQVVKREK
RAVGIGALFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLRAIEAQQHLLQLTVWGIKQLQARVLAVERYLKDQQL
LGLWGCSGKLICTTNVPWNSSWSNKSQEEIWENMTWMEWEKEINNYSNEIYRLIEESQNQQEKNEQELLALDKWASLWNWFD
ISNWLWYIRIFIMIVGGLIGLRIVFAVLSIVNRVRKGYSPLSLQTHIPSPREPDRPEGIEEGGGEQGKDRSVRLVNGFLALI
WDDLRSLCLFSYHRLRDLLLIVTRIVELLGRRGWEVLKYWWNLLQYWSQELKNSAISLLNTTAIVVAEGTDRVIEALQRVGR
AILNIPRRIRQGLERALL$

B

2003 CON_12_BF Env.seq.opt

ATGCGCGTGCGCGGCATGCAGCGCAACTGGCAGCACCTGGGCAAGTGGGGCCTGCTGTTCCTGGGCATCCTGATCATCTGCA
ACGCCACCGAGAACCTGTGGGTGACCGTGTACTACGGCGTGCCCGTGTGGAAGGAGGCCACCACCACCCTGTTCTGCGCCTC
CGACGCCAAGTCCTACGAGCGCGAGGTGCACAACGTGTGGGCCACCCACGCCTGCGTGCCCACCGACCCCAACCCCCAGGAG
GTGGACCTGGAGAACGTGACCGAGAACTTCGACATGTGGAAGAACAACATGGTGGAGCAGATGCACACCGACATCATCTCCC
TGTGGGACCAGTCCCTGAAGCCCTGCGTGAAGCTGACCCCCCTGTGCGTGACCCTGAACTGCACCGACGCCAACGCCACCGC
CAACGCCACCAAGGAGCACCCCGAGGGCCGCGCCGGCGCCATCCAGAACTGCTCCTTCAACATGACCACCGAGGTGCGCGAC
AAGCAGATGAAGGTGCAGGCCCTGTTCTACCGCCTGGACATCGTGCCCATCTCCGACAACAACTCCAACGAGTACCGCCTGA
TCAACTGCAACACCTCCACCATCACCCAGGCCTGCCCCAAGGTGTCCTGGGACCCCATCCCCATCCCACTACTGCGCCCCCGC
CGGCTACGCCATCCTGAAGTGCAACGACAAGAAGTTCAACGGCACCGGCCCCTGCAAGAACGTGTCCACCGTGCAGTGCACC
CACGGCATCAAGCCCGTGGTGTCCACCCAGCTGCTGCTGAACGGCTCCCTGGCCGAGGAGGAGATCATCATCCGCTCCCAGA
ACATCTCCGACAACGCCAAGACCATCATCGTGCACCTGAACGAGTCCGTGCAGATCAACTGCACCCGCCCCAACAACAACAC
CCGCAAGTCCATCCACATCGGCCCCGGCCGCGCCTTCTACGCCACCGGCGACATCATCGGCGACATCCGCAAGGCCCACTGC
AACGTGTCCGGCACCCAGTGGAACAAGACCCTGGAGCAGGTGAAGAAGAAGCTGCGCTCCTACTTCAACACCACCATCAAGT
TCAACTCCTCCTCCGGCGGCGACCCCGAGATCACCATGCACTCCTTCAACTGCCGCGGCGAGTTCTTCTACTGCAACACCTC
CAAGCTGTTCAACGACACCGTGTCCAACGACACCATCATCCTGCCCTGCCGCATCAAGCAGATCGTGAACATGTGGCAGGAG
GTGGGCCGCGCCATGTACGCCGCCCCCATCGCCGGCAACATCACCTGCACCTCCAACATCACCGGCCTGCTGCTGACCCGCG
ACGGCGGCCACAACGAGACCAACAAGACCGAGACCTTCCGCCCCGGCGGCGGCAACATGAAGGACAACTGGCGCTCCGAGCT
GTACAAGTACAAGGTGGTGGAGATCGAGCCCCTGGGCGTGGCCCCCACCCGCGCCAAGCGCCAGGTGGTGAAGCGCGAGAAG
CGCGCCGTGGGCATCGGCGCCCTGTTCCTGGGCTTCCTGGGCGCCGCCGGCTCCACCATGGGCGCCGCCTCCATCACCCTGA
CCGTGCAGGCCCGCCAGCTGCTGTCCGGCATCGTGCAGCAGCAGTCCAACCTGCTGCGCGCCATCGAGGCCCAGCAGCACCT
GCTGCAGCTGACCGTGTGGGGCATCAAGCAGCTGCAGGCCCGCGTGCTGGCCGTGGAGCGCTACCTGAAGGACCAGCAGCTG
CTGGGCCTGTGGGGCTGCTCCGGCAAGCTGATCTGCACCACCAACGTGCCCTGGAACTCCTCCTGGTCCAACAAGTCCCAGG
AGGAGATCTGGGAGAACATGACCTGGATGGAGTGGGAGAAGGAGATCAACAACTACTCCAACGAGATCTACCGCCTGATCGA
GGAGTCCCAGAACCAGCAGGAGAAGAACGAGCAGGAGCTGCTGGCCCTGGACAAGTGGGCCTCCCTGTGGAACTGGTTCGAC
ATCTCCAACTGGCTGTGGTACATCCGCATCTTCATCATGATCGTGGGCGGCCTGATCGGCCTGCGCATCGTGTTCGCCGTGC

TGTCCATCGTGAACCGCGTGCGCAAGGGCTACTCCCCCCTGTCCCTGCAGACCCACATCCCCTCCCCCCGCGAGCCCGACCG
CCCCGAGGGCATCGAGGAGGGCGGCGGCGAGCAGGGCAAGGACCGCTCCGTGCGCCTGGTGAACGGCTTCCTGGCCCTGATC
TGGGACGACCTGCGCTCCCTGTGCCTGTTCTCCTACCACCGCCTGCGCGACCTGCTGCTGATCGTGACCCGCATCGTGGAGC
TGCTGGGCCGCCGCGGCTGGGAGGTGCTGAAGTACTGGTGGAACCTGCTGCAGTACTGGTCCCAGGAGCTGAAGAACTCCGC
CATCTCCCTGCTGAACACCACCGCCATCGTGGTGGCCGAGGGCACCGACCGCGTGATCGAGGCCCTGCAGCGCGTGGGCCGC
GCCATCCTGAACATCCCCCGCCGCATCCGCCAGGGCCTGGAGCGCGCCCTGCTGTAA

9.62A

2003 CON_14_BG Env

MKAKGTQRNWQSLWKWGTLILGLVIICSASNDLWVTVYYGVPVWKEATTTLFCASDAKAYDAEVHNVWATHACVPTDPNPQE
VALENVTENFNMWENNMVDQMQEDIISLWDQSLKPCVELTPLCVTLNCTDFNNTTNNTTNTRNDGEGEIKNCSFNITTSLRD
KIKKEYALFYNLDVVQMDNDNSSYRLTSCNTSIITQACPKVSFTPIPIHYCAPAGFVILKCNNKTFNGTGPCTNVSTVQCTH
GIRPVVSTQLLLNGSLAEEEIVIRSKNFTDNAKTIIVQLKDPIEINCTRPNNNTRKRITMGPGRVLYTTGQIIGDIRKAHCN
ISKTKWNNTLGQIVKKLREQFMNKTIVFQRSSGGDPEIVMHSFNCGGEFFYCNTTQLFNSTWRSNSTWNDTTETNNTDLITL
PCRIKQIVNMWQKVGKAMYAPPISGQIRCSSNITGLLLIRDGGSNNTETFRPGGGNMKDNWRSELYKYKVVKIEPLGVAPTR
AKRRVVQREKRAVGIGALLFGFLGAAGSTMGAASMTLTVQARQLLSGIVQQQNNLLRAIEAQQHMLQLTVWGIKQLQARVLA
VERYLKDQQLLGIWGCSGKLICTTTVPWNASWSNKSLDDIWNNMTWMEWEREIDNYTGLIYTLIEQSQNQQERNEQELLELD
KWASLWNWFNITNWLWYIKIFIMIIGGLIGLRIVFAVLSIINRVRKGYSPLSFQTLTHHQREPDRPGRIEEEGGEQDKDRSI
RLVSGFLALAWDDLRSLCLFSYHRLRDFILIAARTVELLGRSSLKGLRLGWEGLKYLWNLLLYWGRELKNSAINLLDTVAIA
VANWTDRAIEVVQRVGRAVLNIPVRIRQGLERALL$

B

2003 CON_14_BG Env.seq.opt

ATGAAGGCCAAGGGCACCCAGCGCAACTGGCAGTCCCTGTGGAAGTGGGGCACCCTGATCCTGGGCCTGGTGATCATCTGCT
CCGCCTCCAACGACCTGTGGGTGACCGTGTACTACGGCGTGCCCGTGTGGAAGGAGGCCACCACCACCCTGTTCTGCGCCTC
CGACGCCAAGGCCTACGACGCCGAGGTGCACAACGTGTGGGCCACCCACGCCTGCGTGCCCACCGACCCCAACCCCCAGGAG
GTGGCCCTGGAGAACGTGACCGAGAACTTCAACATGTGGGAGAACAACATGGTGGACCAGATGCAGGAGGACATCATCTCCC
TGTGGGACCAGTCCCTGAAGCCCTGCGTGGAGCTGACCCCCCTGTGCGTGACCCTGAACTGCACCGACTTCAACAACACCAC
CAACAACACCACCAACACCCGCAACGACGGCGAGGGCGAGATCAAGAACTGCTCCTTCAACATCACCACCTCCCTGCGCGAC
AAGATCAAGAAGGAGTACGCCCTGTTCTACAACCTGGACGTGGTGCAGATGGACAACGACAACTCCTCCTACCGCCTGACCT
CCTGCAACACCTCCATCATCACCCAGGCCTGCCCCAAGGTGTCCTTCACCCCCATCCCCATCCACTACTGCGCCCCCGCCGG
CTTCGTGATCCTGAAGTGCAACAACAAGACCTTCAACGGCACCGGCCCCTGCACCAACGTGTCCACCGTGCAGTGCACCCAC
GGCATCCGCCCCGTGGTGTCCACCCAGCTGCTGCTGAACGGCTCCCTGGCCGAGGAGGAGATCGTGATCCGCTCCAAGAACT
TCACCGACAACGCCAAGACCATCATCGTGCAGCTGAAGGACCCCATCGAGATCAACTGCACCCGCCCCAACAACAACACCCG
CAAGCGCATCACCATGGGCCCCGGCCGCGTGCTGTACACCACCGGCCAGATCATCGGCGACATCCGCAAGGCCCACTGCAAC
ATCTCCAAGACCAAGTGGAACAACACCCTGGGCCAGATCGTGAAGAAGCTGCGCGAGCAGTTCATGAACAAGACCATCGTGT
TCCAGCGCTCCTCCGGCGGCGACCCCGAGATCGTGATGCACTCCTTCAACTGCGGCGGCGAGTTCTTCTACTGCAACACCAC
CCAGCTGTTCAACTCCACCTGGCGCTCCAACTCCACCTGGAACGACACCACCGAGACCAACAACACCGACCTGATCACCCTG
CCCTGCCGCATCAAGCAGATCGTGAACATGTGGCAGAAGGTGGGCAAGGCCATGTACGCCCCCCCCATCTCCGGCCAGATCC
GCTGCTCCTCCAACATCACCGGCCTGCTGCTGATCCGCGACGGCGGCTCCAACAACACCGAGACCTTCCGCCCCGGCGGCGG
CAACATGAAGGACAACTGGCGCTCCGAGCTGTACAAGTACAAGGTGGTGAAGATCGAGCCCCTGGGCGTGGCCCCCACCCGC
GCCAAGCGCCGCGTGGTGCAGCGCGAGAAGCGCGCCGTGGGCATCGGCGCCCTGCTGTTCGGCTTCCTGGGCGCCGCCGGCT
CCACCATGGGCGCCGCCTCCATGACCCTGACCGTGCAGGCCCGCCAGCTGCTGTCCGGCATCGTGCAGCAGCAGAACAACCT
GCTGCGCGCCATCGAGGCCCAGCAGCACATGCTGCAGCTGACCGTGTGGGGCATCAAGCAGCTGCAGGCCCGCGTGCTGGCC
GTGGAGCGCTACCTGAAGGACCAGCAGCTGCTGGGCATCTGGGGCTGCTCCGGCAAGCTGATCTGCACCACCACCGTGCCCT
GGAACGCCTCCTGGTCCAACAAGTCCCTGGACGACATCTGGAACAACATGACCTGGATGGAGTGGGAGCGCGAGATCGACAA
CTACACCGGCCTGATCTACACCCTGATCGAGCAGTCCCAGAACCAGCAGGAGCGCAACGAGCAGGAGCTGCTGGAGCTGGAC
AAGTGGGCCTCCCTGTGGAACTGGTTCAACATCACCAACTGGCTGTGGTACATCAAGATCTTCATCATGATCATCGGCGGCC
TGATCGGCCTGCGCATCGTGTTCGCCGTGCTGTCCATCATCAACCGCGTGCGCAAGGGCTACTCCCCCCTGTCCTTCCAGAC
CCTGACCCACCACCAGCGCGAGCCCGACCGCCCCGGCCGCATCGAGGAGGAGGGCGGCGAGCAGGACAAGGACCGCTCCATC
CGCCTGGTGTCCGGCTTCCTGGCCCTGGCCTGGGACGACCTGCGCTCCCTGTGCCTGTTCTCCTACCACCGCCTGCGCGACT
TCATCCTGATCGCCGCCCGCACCGTGGAGCTGCTGGGCCGCTCCTCCCTGAAGGGCCTGCGCCTGGGCTGGGAGGGCCTGAA
GTACCTGTGGAACCTGCTGCTGTACTGGGGCCGCGAGCTGAAGAACTCCGCCATCAACCTGCTGGACACCGTGGCCATCGCC
GTGGCCAACTGGACCGACCGCGCCATCGAGGTGGTGCAGCGCGTGGGCCGCGCCGTGCTGAACATCCCCGTGCGCATCCGCC
AGGGCCTGGAGCGCGCCCTGCTGTAA

Centralized HIV-1 gag/nef/pol Protein and the Codon-optimized Gene Sequences

Fig. 63

A

1. 2003_CON_S gag.PEP

MGARASVLSGGKLDAWEKIRLRPGGKKKYRLKHLVWASRELERFALNPGLLETSEGCQQIIEQLQPALQTGSEELRSLYNTV
ATLYCVHQRIEVKDTKEALDKIEEEQNKSKQKTQQAAADTGNSSKVSQNYPIVQNLQGQMVHQAISPRTLNAWVKVVEEKAF
SPEVIPMFSALSEGATPQDLNTMLNTVGGHQAAMQMLKDTINEEAAEWDRLHPVHAGPIPPGQMREPRGSDIAGTTSTLQEQ
IGWMTSNPPIPVGEIYKRWIILGLNKIVRMYSPVSILDIRQGPKEPFRDYVDRFFKTLRAEQATQDVKNWMTDTLLVQNANP
DCKTILKALGPGATLEEMMTACQGVGGPSHKARVLAEAMSQVTNTTIMMQRGNFKGQKRIIKCFNCGKEGHIARNCRAPRKK
GCWKCGKEGHQMKDCTERQANFLGKIWPSNKGRPGNFLQSRPEPTAPPAESFGFGEEITPSPKQEPKDKELYPLASLKSLFG
NDPLSQ$

B

2003_CON_S gag.OPT

ATGGGCGCCCGCGCCTCCGTGCTGTCCGGCGGCAAGCTGGACGCCTGGGAGAAGATCCGCCTGCGCCCCGGCGGCAAGAAGA
AGTACCGCCTGAAGCACCTGGTGTGGGCCTCCCGCGAGCTGGAGCGCTTCGCCCTGAACCCCGGCCTGCTGGAGACCTCCGA
GGGCTGCCAGCAGATCATCGAGCAGCTGCAGCCCGCCCTGCAGACCGGCTCCGAGGAGCTGCGCTCCCTGTACAACACCGTG
GCCACCCTGTACTGCGTGCACCAGCGCATCGAGGTGAAGGACACCAAGGAGGCCCTGGACAAGATCGAGGAGGAGCAGAACA
AGTCCAAGCAGAAGACCCAGCAGGCCGCCGCCGACACCGGCAACTCCTCCAAGGTGTCCCAGAACTACCCCATCGTGCAGAA
CCTGCAGGGCCAGATGGTGCACCAGGCCATCTCCCCCCGCACCCTGAACGCCTGGGTGAAGGTGGTGGAGGAGAAGGCCTTC
TCCCCCGAGGTGATCCCCATGTTCTCCGCCCTGTCCGAGGGCGCCACCCCCCAGGACCTGAACACCATGCTGAACACCGTGG
GCGGCCACCAGGCCGCCATGCAGATGCTGAAGGACACCATCAACGAGGAGGCCGCCGAGTGGGACCGCCTGCACCCCGTGCA
CGCCGGCCCCATCCCCCCCGGCCAGATGCGCGAGCCCCGCGGCTCCGACATCGCCGGCACCACCTCCACCCTGCAGGAGCAG
ATCGGCTGGATGACCTCCAACCCCCCCATCCCCGTGGGCGAGATCTACAAGCGCTGGATCATCCTGGGCCTGAACAAGATCG
TGCGCATGTACTCCCCCGTGTCCATCCTGGACATCCGCCAGGGCCCCAAGGAGCCCTTCCGCGACTACGTGGACCGCTTCTT
CAAGACCCTGCGCGCCGAGCAGGCCACCCAGGACGTGAAGAACTGGATGACCGACACCCTGCTGGTGCAGAACGCCAACCCC
GACTGCAAGACCATCCTGAAGGCCCTGGGCCCCGGCGCCACCCTGGAGGAGATGATGACCGCCTGCCAGGGCGTGGGCGGCC
CCTCCCACAAGGCCCGCGTGCTGGCCGAGGCCATGTCCCAGGTGACCAACACCACCATCATGATGCAGCGCGGCAACTTCAA
GGGCCAGAAGCGCATCATCAAGTGCTTCAACTGCGGCAAGGAGGGCCACATCGCCCGCAACTGCCGCGCCCCCCGCAAGAAG
GGCTGCTGGAAGTGCGGCAAGGAGGGCCACCAGATGAAGGACTGCACCGAGCGCCAGGCCAACTTCCTGGGCAAGATCTGGC
CCTCCAACAAGGGCCGCCCCGGCAACTTCCTGCAGTCCCGCCCCGAGCCCACCGCCCCCCCCGCCGAGTCCTTCGGCTTCGG
CGAGGAGATCACCCCCTCCCCCAAGCAGGAGCCCAAGGACAAGGAGCTGTACCCCCTGGCCTCCCTGAAGTCCCTGTTCGGC
AACGACCCCCTGTCCCAGTAA

Fig. 64

A

2. 2003_M.GROUP.anc gag.PEP

MGARASVLSGGKLDAWEKIRLRPGGKKKYRLKHLVWASRELERFALNPGLLETAEGCQQIMGQLQPALQTGTEELRSLYNTV
ATLYCVHQRIEVKDTKEALDKIEEEQNKSQQKTQQAAADKGDSSQVSQNYPIVQNLQGQMVHQAISPRTLNAWVKVVEEKAF
SPEVIPMFSALSEGATPQDLNTMLNTVGGHQAAMQMLKDTINEEAAEWDRLHPVHAGPIPPGQMREPRGSDIAGTTSTLQEQ
IGWMTSNPPIPVGEIYKRWIILGLNKIVRMYSPVSILDIRQGPKEPFRDYVDRFFKTLRAEQATQDVKNWMTDTLLVQNANP
DCKTILKALGPGATLEEMMTACQGVGGPGHKARVLAEAMSQVTNANIMMQRGNFKGPRRIVKCFNCGKEGHIARNCRAPRKK
GCWKCGKEGHQMKDCTERQANFLGKIWPSNKGRPGNFLQSRPEPTAPPAESFGFGEEITPSPKQEPKDKELYPLASLKSLFG
SDPLSQ$

B

2003_M.GROUP.anc gag.OPT

ATGGGCGCCCGCGCCTCCGTGCTGTCCGGCGGCAAGCTGGACGCCTGGGAGAAGATCCGCCTGCGCCCCGGCGGCAAGAAGA
AGTACCGCCTGAAGCACCTGGTGTGGGCCTCCCGCGAGCTGGAGCGCTTCGCCCTGAACCCCGGCCTGCTGGAGACCGCCGA
GGGCTGCCAGCAGATCATGGGCCAGCTGCAGCCCGCCCTGCAGACCGGCACCGAGGAGCTGCGCTCCCTGTACAACACCGTG
GCCACCCTGTACTGCGTGCACCAGCGCATCGAGGTGAAGGACACCAAGGAGGCCCTGGACAAGATCGAGGAGGAGCAGAACA
AGTCCCAGCAGAAGACCCAGCAGGCCGCCGCCGACAAGGGCGACTCCTCCCAGGTGTCCCAGAACTACCCCATCGTGCAGAA
CCTGCAGGGCCAGATGGTGCACCAGGCCATCTCCCCCCGCACCCTGAACGCCTGGGTGAAGGTGGTGGAGGAGAAGGCCTTC
TCCCCCGAGGTGATCCCCATGTTCTCCGCCCTGTCCGAGGGCGCCACCCCCCAGGACCTGAACACCATGCTGAACACCGTGG
GCGGCCACCAGGCCGCCATGCAGATGCTGAAGGACACCATCAACGAGGAGGCCGCCGAGTGGGACCGCCTGCACCCCGTGCA
CGCCGGCCCCATCCCCCCCGGCCAGATGCGCGAGCCCCGCGGCTCCGACATCGCCGGCACCACCTCCACCCTGCAGGAGCAG
ATCGGCTGGATGACCTCCAACCCCCCCATCCCCGTGGGCGAGATCTACAAGCGCTGGATCATCCTGGGCCTGAACAAGATCG
TGCGCATGTACTCCCCCGTGTCCATCCTGGACATCCGCCAGGGCCCCAAGGAGCCCTTCCGCGACTACGTGGACCGCTTCTT
CAAGACCCTGCGCGCCGAGCAGGCCACCCAGGACGTGAAGAACTGGATGACCGACACCCTGCTGGTGCAGAACGCCAACCCC
GACTGCAAGACCATCCTGAAGGCCCTGGGCCCCGGCGCCACCCTGGAGGAGATGATGACCGCCTGCCAGGGCGTGGGCGGCC
CCGGCCACAAGGCCCGCGTGCTGGCCGAGGCCATGTCCCAGGTGACCAACGCCAACATCATGATGCAGCGCGGCAACTTCAA
GGGCCCCCGCCGCATCGTGAAGTGCTTCAACTGCGGCAAGGAGGGCCACATCGCCCGCAACTGCCGCGCCCCCCGCAAGAAG

GGCTGCTGGAAGTGCGGCAAGGAGGGCCACCAGATGAAGGACTGCACCGAGCGCCAGGCCAACTTCCTGGGCAAGATCTGGC
CCTCCAACAAGGGCCGCCCCGGCAACTTCCTGCAGTCCCGCCCCGAGCCCACCGCCCCCCCCGCCGAGTCCTTCGGCTTCGG
CGAGGAGATCACCCCCTCCCCCAAGCAGGAGCCCAAGGACAAGGAGCTGTACCCCCTGGCCTCCCTGAAGTCCCTGTTCGGC
TCCGACCCCCTGTCCCAGTAA

Fig. 65

A

3. 2003_CON_A1 gag.PEP

MGARASVLSGGKLDAWEKIRLRPGGKKKYRLKHLVWASRELERFALNPSLLETTEGCQQIMEQLQPALKTGTEELRSLYNTV
ATLYCVHQRIDVKDTKEALDKIEEIQNKSKQKTQQAAADTGNSSKVSQNYPIVQNAQGQMVHQSLSPRTLNAWVKVIEEKAF
SPEVIPMFSALSEGATPQDLNMMLNIVGGHQAAMQMLKDTINEEAAEWDRLHPVHAGPIPPGQMREPRGSDIAGTTSTPQEQ
IGWMTGNPPIPVGDIYKRWIILGLNKIVRMYSPVSILDIKQGPKEPFRDYVDRFFKTLRAEQATQEVKNWMTETLLVQNANP
DCKSILRALGPGATLEEMMTACQGVGGPGHKARVLAEAMSQVQHTNIMMQRGNFRGQKRIKCFNCGKEGHLARNCRAPRKKG
CWKCGKEGHQMKDCTERQANFLGKIWPSSKGRPGNFPQSRPEPTAPPAEIFGMGEEITSPPKQEQKDREQDPPLVSLKSLFG
NDPLSQ$

B

3. 2003_CON_A1 gag.OPT

ATGGGCGCCCGCGCCTCCGTGCTGTCCGGCGGCAAGCTGGACGCCTGGGAGAAGATCCGCCTGCGCCCCGGCGGCAAGAAGA
AGTACCGCCTGAAGCACCTGGTGTGGGCCTCCCGCGAGCTGGAGCGCTTCGCCCTGAACCCCTCCCTGCTGGAGACCACCGA
GGGCTGCCAGCAGATCATGGAGCAGCTGCAGCCCGCCCTGAAGACCGGCACCGAGGAGCTGCGCTCCCTGTACAACACCGTG
GCCACCCTGTACTGCGTGCACCAGCGCATCGACGTGAAGGACACCAAGGAGGCCCTGGACAAGATCGAGGAGATCCAGAACA
AGTCCAAGCAGAAGACCCAGCAGGCCGCCGCCGACACCGGCAACTCCTCCAAGGTGTCCCAGAACTACCCCATCGTGCAGAA
CGCCCAGGGCCAGATGGTGCACCAGTCCCTGTCCCCCCGCACCCTGAACGCCTGGGTGAAGGTGATCGAGGAGAAGGCCTTC
TCCCCCGAGGTGATCCCCATGTTCTCCGCCCTGTCCGAGGGCGCCACCCCCCAGGACCTGAACATGATGCTGAACATCGTGG
GCGGCCACCAGGCCGCCATGCAGATGCTGAAGGACACCATCAACGAGGAGGCCGCCGAGTGGGACCGCCTGCACCCCGTGCA
CGCCGGCCCCATCCCCCCCCGGCCAGATGCGCGAGCCCCGCGGCTCCGACATCGCCGGCACCACCTCCACCCCCCAGGAGCAG
ATCGGCTGGATGACCGGCAACCCCCCCCATCCCCGTGGGCGACATCTACAAGCGCTGGATCATCCTGGGCCTGAACAAGATCG
TGCGCATGTACTCCCCCGTGTCCATCCTGGACATCAAGCAGGGCCCCAAGGAGCCCTTCCGCGACTACGTGGACCGCTTCTT
CAAGACCCTGCGCGCCGAGCAGGCCACCCAGGAGGTGAAGAACTGGATGACCGAGACCCTGCTGGTGCAGAACGCCAACCCC
GACTGCAAGTCCATCCTGCGCGCCCTGGGCCCCGGCGCCACCCTGGAGGAGATGATGACCGCCTGCCAGGGCGTGGGCGGCC
CCGGCCACAAGGCCCGCGTGCTGGCCGAGGCCATGTCCCAGGTGCAGCACACCAACATCATGATGCAGCGCGGCAACTTCCG
CGGCCAGAAGCGCATCAAGTGCTTCAACTGCGGCAAGGAGGGCCACCTGGCCCGCAACTGCCGCGCCCCCCGCAAGAAGGGC
TGCTGGAAGTGCGGCAAGGAGGGCCACCAGATGAAGGACTGCACCGAGCGCCAGGCCAACTTCCTGGGCAAGATCTGGCCCT
CCTCCAAGGGCCGCCCCGGCAACTTCCCCCAGTCCCGCCCCGAGCCCACCGCCCCCCCCGCCGAGATCTTCGGCATGGGCGA
GGAGATCACCTCCCCCCCCAAGCAGGAGCAGAAGGACCGCGAGCAGGACCCCCCCCTGGTGTCCCTGAAGTCCCTGTTCGGC
AACGACCCCCTGTCCCAGTAA

C

4. 2003_A1.anc gag.PEP

MGARASVLSGGKLDAWEKIRLRPGGKKKYRLKHLVWASRELERFALNPGLLETAEGCQQIMGQLQPALKTGTEELRSLYNTV
ATLYCVHQRIEVKDTKEALDKIEEIQNKSKQKTQQAAADTGNSSKVSQNYPIVQNAQGQMVHQSLSPRTLNAWVKVIEEKAF
SPEVIPMFSALSEGATPQDLNMMLNIVGGHQAAMQMLKDTINEEAAEWDRLHPVHAGPIPPGQMREPRGSDIAGTTSTLQEQ
IGWMTGNPPIPVGDIYKRWIILGLNKIVRMYSPVSILDIRQGPKEPFRDYVDRFFKTLRAEQATQEVKNWMTETLLVQNANP
DCKSILRALGPGATLEEMMTACQGVGGPGHKARVLAEAMSQVQNTDIMMQRGNFRGPKRIKCFNCGKEGHLARNCRAPRKKG
CWKCGKEGHQMKDCTERQANFLGKIWPSSKGRPGNFPQSRPEPTAPPAENFGMGEEMISSPKQEQKDREQYPPLVSLKSLFG
NDPLSQ$

D

2003_A1.anc gag.OPT

ATGGGCGCCCGCGCCTCCGTGCTGTCCGGCGGCAAGCTGGACGCCTGGGAGAAGATCCGCCTGCGCCCCGGCGGCAAGAAGA
AGTACCGCCTGAAGCACCTGGTGTGGGCCTCCCGCGAGCTGGAGCGCTTCGCCCTGAACCCCGGCCTGCTGGAGACCGCCGA
GGGCTGCCAGCAGATCATGGGCCAGCTGCAGCCCGCCCTGAAGACCGGCACCGAGGAGCTGCGCTCCCTGTACAACACCGTG
GCCACCCTGTACTGCGTGCACCAGCGCATCGAGGTGAAGGACACCAAGGAGGCCCTGGACAAGATCGAGGAGATCCAGAACA
AGTCCAAGCAGAAGACCCAGCAGGCCGCCGCCGACACCGGCAACTCCTCCAAGGTGTCCCAGAACTACCCCATCGTGCAGAA
CGCCCAGGGCCAGATGGTGCACCAGTCCCTGTCCCCCCGCACCCTGAACGCCTGGGTGAAGGTGATCGAGGAGAAGGCCTTC
TCCCCCGAGGTGATCCCCATGTTCTCCGCCCTGTCCGAGGGCGCCACCCCCCAGGACCTGAACATGATGCTGAACATCGTGG
GCGGCCACCAGGCCGCCATGCAGATGCTGAAGGACACCATCAACGAGGAGGCCGCCGAGTGGGACCGCCTGCACCCCGTGCA
CGCCGGCCCCATCCCCCCCCGGCCAGATGCGCGAGCCCCGCGGCTCCGACATCGCCGGCACCACCTCCACCCTGCAGGAGCAG
ATCGGCTGGATGACCGGCAACCCCCCCCATCCCCGTGGGCGACATCTACAAGCGCTGGATCATCCTGGGCCTGAACAAGATCG
TGCGCATGTACTCCCCCGTGTCCATCCTGGACATCCGCCAGGGCCCCAAGGAGCCCTTCCGCGACTACGTGGACCGCTTCTT
CAAGACCCTGCGCGCCGAGCAGGCCACCCAGGAGGTGAAGAACTGGATGACCGAGACCCTGCTGGTGCAGAACGCCAACCCC
GACTGCAAGTCCATCCTGCGCGCCCTGGGCCCCGGCGCCACCCTGGAGGAGATGATGACCGCCTGCCAGGGCGTGGGCGGCC

CCGGCCACAAGGCCCCGCGTGCTGGCCGAGGCCATGTCCCAGGTGCAGAACACCGACATCATGATGCAGCGCGGCAACTTCCG
CGGCCCCAAGCGCATCAAGTGCTTCAACTGCGGCAAGGAGGGCCACCTGGCCCGCAACTGCCGCGCCCCCCGCAAGAAGGGC
TGCTGGAAGTGCGGCAAGGAGGGCCACCAGATGAAGGACTGCACCGAGCGCCAGGCCAACTTCCTGGGCAAGATCTGGCCCT
CCTCCAAGGGCCGCCCCGGCAACTTCCCCCAGTCCCGCCCCGAGCCCACCGCCCCCCCCGCCGAGAACTTCGGCATGGGCGA
GGAGATGATCTCCTCCCCCAAGCAGGAGCAGAAGGACCGCGAGCAGTACCCCCCCCCTGGTGTCCCTGAAGTCCCTGTTCGGC
AACGACCCCCTGTCCCAGTAA

Fig. 66

5. 2003_CON_A2 gag.PEP

A

MGARASILSGGKLDAWEKIRLRPGGKKKYRLKHLVWASRELEKFSINPSLLETSEGCRQIIRQLQPALQTGTEELKSLYNTV
AVLYCVHQRIDVKDTKEALDKIEEEQNKCKQKTQHAAADTGNSSSSSQNYPIVQNAQGQMVHQAISPRTLNAWVKVVEEKAF
SPEVIPMFTALSEGATPQDLNTMLNTVGGHQAAMQMLKDTINEEAAEWDRLHPVHAGPIPPGQMREPRGSDIAGTTSTLQÈQ
IGWMTSNPPIPVGEIYKRWIILGLNKIVRMYSPVSILDIRQGPKEPFRDYVDRFFKTLRAEQATQEVKNWMTDTLLVQNANP
DCKSILRALGPGATLEEMMTACQGVGGPSHKARVLAEAMSQVQNTNTNIMMQRGNFRGQKRIKCFNCGKEGHLARNCRAPRK
KGCWKCGKEGHQMKDCTERQANFLGKIWPSNKGRPGNFPQSRTEPTAPPAENLRMGEEITSSLKQELKTREPYNPAISLKSL
FGNDPLSQ$

B

2003_CON_A2 gag.OPT

ATGGGCGCCCGCGCCTCCATCCTGTCCGGCGGCAAGCTGGACGCCTGGGAGAAGATCCGCCTGCGCCCCGGCGGCAAGAAGA
AGTACCGCCTGAAGCACCTGGTGTGGGCCTCCCGCGAGCTGGAGAAGTTCTCCATCAACCCCTCCCTGCTGGAGACCTCCGA
GGGCTGCCGCCAGATCATCCGCCAGCTGCAGCCCGCCCTGCAGACCGGCACCGAGGAGCTGAAGTCCCTGTACAACACCGTG
GCCGTGCTGTACTGCGTGCACCAGCGCATCGACGTGAAGGACACCAAGGAGGCCCTGGACAAGATCGAGGAGGAGCAGAACA
AGTGCAAGCAGAAGACCCAGCACGCCGCCGCCGACACCGGCAACTCCTCCTCCTCCTCCCAGAACTACCCCATCGTGCAGAA
CGCCCAGGGCCAGATGGTGCACCAGGCCATCTCCCCCCGCACCCTGAACGCCTGGGTGAAGGTGGTGGAGGAGAAGGCCTTC
TCCCCCGAGGTGATCCCCATGTTCACCGCCCTGTCCGAGGGCGCCACCCCCCAGGACCTGAACACCATGCTGAACACCGTGG
GCGGCCACCAGGCCGCCATGCAGATGCTGAAGGACACCATCAACGAGGAGGCCGCCGAGTGGGACCGCCTGCACCCCGTGCA
CGCCGGCCCCATCCCCCCCGGCCAGATGCGCGAGCCCCGCGGCTCCGACATCGCCGGCACCACCTCCACCCTGCAGGAGCAG
ATCGGCTGGATGACCTCCAACCCCCCCCATCCCCGTGGGCGAGATCTACAAGCGCTGGATCATCCTGGGCCTGAACAAGATCG
TGCGCATGTACTCCCCCGTGTCCATCCTGGACATCCGCCAGGGCCCCAAGGAGCCCTTCCGCGACTACGTGGACCGCTTCTT
CAAGACCCTGCGCGCCGAGCAGGCCACCCAGGAGGTGAAGAACTGGATGACCGACACCCTGCTGGTGCAGAACGCCAACCCC
GACTGCAAGTCCATCCTGCGCGCCCTGGGCCCCGGCGCCACCCTGGAGGAGATGATGACCGCCTGCCAGGGCGTGGGCGGCC
CCTCCCACAAGGCCCGCGTGCTGGCCGAGGCCATGTCCCAGGTGCAGAACACCAACACCAACATCATGATGCAGCGCGGCAA
CTTCCGCGGCCAGAAGCGCATCAAGTGCTTCAACTGCGGCAAGGAGGGCCACCTGGCCCGCAACTGCCGCGCCCCCCGCAAG
AAGGGCTGCTGGAAGTGCGGCAAGGAGGGCCACCAGATGAAGGACTGCACCGAGCGCCAGGCCAACTTCCTGGGCAAGATCT
GGCCCTCCAACAAGGGCCGCCCCGGCAACTTCCCCCAGTCCCGCACCGAGCCCACCGCCCCCCCCCGCCGAGAACCTGCGCAT
GGGCGAGGAGATCACCTCCTCCCTGAAGCAGGAGCTGAAGACCCGCGAGCCCTACAACCCCGCCATCTCCCTGAAGTCCCTG
TTCGGCAACGACCCCCTGTCCCAGTAA

Fig. 67

6. 2003_CON_B gag.PEP

A

MGARASVLSGGELDRWEKIRLRPGGKKKYKLKHIVWASRELERFAVNPGLLETSEGCRQILGQLQPSLQTGSEELRSLYNTV
ATLYCVHQRIEVKDTKEALEKIEEEQNKSKKKAQQAAADTGNSSQVSQNYPIVQNLQGQMVHQAISPRTLNAWVKVVEEKAF
SPEVIPMFSALSEGATPQDLNTMLNTVGGHQAAMQMLKETINEEAAEWDRLHPVHAGPIAPGQMREPRGSDIAGTTSTLQEQ
IGWMTNNPPIPVGEIYKRWIILGLNKIVRMYSPTSILDIRQGPKEPFRDYVDRFYKTLRAEQASQEVKNWMTETLLVQNANP
DCKTILKALGPAATLEEMMTACQGVGGPGHKARVLAEAMSQVTNSATIMMQRGNFRNQRKTVKCFNCGKEGHIAKNCRAPRK
KGCWKCGKEGHQMKDCTERQANFLGKIWPSHKGRPGNFLQSRPEPTAPPEESFRFGEETTTPSQKQEPIDKELYPLAS$

B

2003_CON_B gag.OPT

ATGGGCGCCCGCGCCTCCGTGCTGTCCGGCGGCGAGCTGGACCGCTGGGAGAAGATCCGCCTGCGCCCCGGCGGCAAGAAGA
AGTACAAGCTGAAGCACATCGTGTGGGCCTCCCGCGAGCTGGAGCGCTTCGCCGTGAACCCCGGCCTGCTGGAGACCTCCGA
GGGCTGCCGCCAGATCCTGGGCCAGCTGCAGCCCTCCCTGCAGACCGGCTCCGAGGAGCTGCGCTCCCTGTACAACACCGTG
GCCACCCTGTACTGCGTGCACCAGCGCATCGAGGTGAAGGACACCAAGGAGGCCCTGGAGAAGATCGAGGAGGAGCAGAACA
AGTCCAAGAAGAAGGCCCAGCAGGCCGCCGCCGACACCGGCAACTCCTCCCAGGTGTCCCAGAACTACCCCATCGTGCAGAA
CCTGCAGGGCCAGATGGTGCACCAGGCCATCTCCCCCCGCACCCTGAACGCCTGGGTGAAGGTGGTGGAGGAGAAGGCCTTC
TCCCCCGAGGTGATCCCCATGTTCTCCGCCCTGTCCGAGGGCGCCACCCCCCAGGACCTGAACACCATGCTGAACACCGTGG
GCGGCCACCAGGCCGCCATGCAGATGCTGAAGGAGACCATCAACGAGGAGGCCGCCGAGTGGGACCGCCTGCACCCCGTGCA
CGCCGGCCCCATCGCCCCCGGCCAGATGCGCGAGCCCCGCGGCTCCGACATCGCCGGCACCACCTCCACCCTGCAGGAGCAG
ATCGGCTGGATGACCAACAACCCCCCCATCCCCGTGGGCGAGATCTACAAGCGCTGGATCATCCTGGGCCTGAACAAGATCG
TGCGCATGTACTCCCCCACCTCCATCCTGGACATCCGCCAGGGCCCCAAGGAGCCCTTCCGCGACTACGTGGACCGCTTCTA
CAAGACCCTGCGCGCCGAGCAGGCCTCCCAGGAGGTGAAGAACTGGATGACCGAGACCCTGCTGGTGCAGAACGCCAACCCC
GACTGCAAGACCATCCTGAAGGCCCTGGGCCCCGCCGCCACCCTGGAGGAGATGATGACCGCCTGCCAGGGCGTGGGCGGCC

CCGGCCACAAGGCCCGCGTGCTGGCCGAGGCCATGTCCCAGGTGACCAACTCCGCCACCATCATGATGCAGCGCGGCAACTT
CCGCAACCAGCGCAAGACCGTGAAGTGCTTCAACTGCGGCAAGGAGGGCCACATCGCCAAGAACTGCCGCGCCCCCCGCAAG
AAGGGCTGCTGGAAGTGCGGCAAGGAGGGCCACCAGATGAAGGACTGCACCGAGCGCCAGGCCAACTTCCTGGGCAAGATCT
GGCCCTCCCACAAGGGCCGCCCCGGCAACTTCCTGCAGTCCCGCCCCGAGCCCACCGCCCCCCCCGAGGAGTCCTTCCGCTT
CGGCGAGGAGACCACCACCCCCTCCCAGAAGCAGGAGCCCATCGACAAGGAGCTGTACCCCCTGGCCTCCTAA

C

7. 2003_B.anc gag.PEP
MGARASVLSGGKLDKWEKIRLRPGGKKKYKLKHIVWASRELERFAVNPGLLETSEGCRQILGQLQPALQTGSEELRSLYNTV
ATLYCVHQRIEVKDTKEALDKIEEEQNKSKKKAQQAAADTGNSSQVSQNYPIVQNLQGQMVHQAISPRTLNAWVKVVEEKAF
SPEVIPMFSALSEGATPQDLNTMLNTVGGHQAAMQMLKETINEEAAEWDRLHPVHAGPIAPGQMREPRGSDIAGTTSTLQEQ
IGWMTNNPPIPVGEIYKRWIILGLNKIVRMYSPISILDIRQGPKEPFRDYVDRFYKTLRAEQASQDVKNWMTETLLVQNANP
DCKTILKALGPAATLEEMMTACQGVGGPGHKARVLAEAMSQVTNSTTIMMQRGNFRDQRKIVKCFNCGKEGHIARNCRAPRK
KGCWKCGKEGHQMKDCTERQANFLGKIWPSHKGRPGNFLQSRPEPTAPPEESFRFGEETTTPSQKQEPIDKELYPLASLKSL
FGNDPSSQ$

D

2003_B.anc gag.OPT
ATGGGCGCCCGCGCCTCCGTGCTGTCCGGCGGCAAGCTGGACAAGTGGGAGAAGATCCGCCTGCGCCCCGGCGGCAAGAAGA
AGTACAAGCTGAAGCACATCGTGTGGGCCTCCCGCGAGCTGGAGCGCTTCGCCGTGAACCCCGGCCTGCTGGAGACCTCCGA
GGGCTGCCGCCAGATCCTGGGCCAGCTGCAGCCCGCCCTGCAGACCGGCTCCGAGGAGCTGCGCTCCCTGTACAACACCGTG
GCCACCCTGTACTGCGTGCACCAGCGCATCGAGGTGAAGGACACCAAGGAGGCCCTGGACAAGATCGAGGAGGAGCAGAACA
AGTCCAAGAAGAAGGCCCAGCAGGCCGCCGCCGACACCGGCAACTCCTCCCAGGTGTCCCAGAACTACCCCATCGTGCAGAA
CCTGCAGGGCCAGATGGTGCACCAGGCCATCTCCCCCCGCACCCTGAACGCCTGGGTGAAGGTGGTGGAGGAGAAGGCCTTC
TCCCCCGAGGTGATCCCCATGTTCTCCGCCCTGTCCGAGGGCGCCACCCCCCAGGACCTGAACACCATGCTGAACACCGTGG
GCGGCCACCAGGCCGCCATGCAGATGCTGAAGGAGACCATCAACGAGGAGGCCGCCGAGTGGGACCGCCTGCACCCCGTGCA
CGCCGGCCCCATCGCCCCCGGCCAGATGCGCGAGCCCCGCGGCTCCGACATCGCCGGCACCACCTCCACCCTGCAGGAGCAG
ATCGGCTGGATGACCAACAACCCCCCCATCCCCGTGGGCGAGATCTACAAGCGCTGGATCATCCTGGGCCTGAACAAGATCG
TGCGCATGTACTCCCCCATCTCCATCCTGGACATCCGCCAGGGCCCCAAGGAGCCCTTCCGCGACTACGTGGACCGCTTCTA
CAAGACCCTGCGCGCCGAGCAGGCCTCCCAGGACGTGAAGAACTGGATGACCGAGACCCTGCTGGTGCAGAACGCCAACCCC
GACTGCAAGACCATCCTGAAGGCCCTGGGCCCCGCCGCCACCCTGGAGGAGATGATGACCGCCTGCCAGGGCGTGGGCGGCC
CCGGCCACAAGGCCCGCGTGCTGGCCGAGGCCATGTCCCAGGTGACCAACTCCACCACCATCATGATGCAGCGCGGCAACTT
CCGCGACCAGCGCAAGATCGTGAAGTGCTTCAACTGCGGCAAGGAGGGCCACATCGCCCGCAACTGCCGCGCCCCCCGCAAG
AAGGGCTGCTGGAAGTGCGGCAAGGAGGGCCACCAGATGAAGGACTGCACCGAGCGCCAGGCCAACTTCCTGGGCAAGATCT
GGCCCTCCCACAAGGGCCGCCCCGGCAACTTCCTGCAGTCCCGCCCCGAGCCCACCGCCCCCCCCGAGGAGTCCTTCCGCTT
CGGCGAGGAGACCACCACCCCCTCCCAGAAGCAGGAGCCCATCGACAAGGAGCTGTACCCCCTGGCCTCCCTGAAGTCCCTG
TTCGGCAACGACCCCTCCTCCCAGTAA

Fig. 68

8. 2003_CON_C gag.PEP
MGARASILRGGKLDKWEKIRLRPGGKKHYMLKHLVWASRELERFALNPGLLETSEGCKQIIKQLQPALQTGTEELRSLYNTV
ATLYCVHEKIEVRDTKEALDKIEEEQNKSQQKTQQAKAADGKVSQNYPIVQNLQGQMVHQAISPRTLNAWVKVIEEKAFSPE
VIPMFTALSEGATPQDLNTMLNTVGGHQAAMQMLKDTINEEAAEWDRLHPVHAGPIAPGQMREPRGSDIAGTTSTLQEQIAW
MTSNPPIPVGDIYKRWIILGLNKIVRMYSPVSILDIKQGPKEPFRDYVDRFFKTLRAEQATQDVKNWMTDTLLVQNANPDCK
TILRALGPGATLEEMMTACQGVGGPSHKARVLAEAMSQANNTNIMMQRSNFKGPKRIVKCFNCGKEGHIARNCRAPRKKGCW
KCGKEGHQMKDCTERQANFLGKIWPSHKGRPGNFLQNRPEPTAPPAESFRFEETTPAPKQEPKDREPLTSLKSLFGSDPLSQ
$

B

2003_CON_C gag.OPT
ATGGGCGCCCGCGCCTCCATCCTGCGCGGCGGCAAGCTGGACAAGTGGGAGAAGATCCGCCTGCGCCCCGGCGGCAAGAAGC
ACTACATGCTGAAGCACCTGGTGTGGGCCTCCCGCGAGCTGGAGCGCTTCGCCCTGAACCCCGGCCTGCTGGAGACCTCCGA
GGGCTGCAAGCAGATCATCAAGCAGCTGCAGCCCGCCCTGCAGACCGGCACCGAGGAGCTGCGCTCCCTGTACAACACCGTG
GCCACCCTGTACTGCGTGCACGAGAAGATCGAGGTGCGCGACACCAAGGAGGCCCTGGACAAGATCGAGGAGGAGCAGAACA
AGTCCCAGCAGAAGACCCAGCAGGCCAAGGCCGCCGACGGCAAGGTGTCCCAGAACTACCCCATCGTGCAGAACCTGCAGGG
CCAGATGGTGCACCAGGCCATCTCCCCCCGCACCCTGAACGCCTGGGTGAAGGTGATCGAGGAGAAGGCCTTCTCCCCCGAG
GTGATCCCCATGTTCACCGCCCTGTCCGAGGGCGCCACCCCCCAGGACCTGAACACCATGCTGAACACCGTGGGCGGCCACC
AGGCCGCCATGCAGATGCTGAAGGACACCATCAACGAGGAGGCCGCCGAGTGGGACCGCCTGCACCCCGTGCACGCCGGCCC
CATCGCCCCCGGCCAGATGCGCGAGCCCCGCGGCTCCGACATCGCCGGCACCACCTCCACCCTGCAGGAGCAGATCGCCTGG
ATGACCTCCAACCCCCCCATCCCCGTGGGCGACATCTACAAGCGCTGGATCATCCTGGGCCTGAACAAGATCGTGCGCATGT
ACTCCCCCGTGTCCATCCTGGACATCAAGCAGGGCCCCAAGGAGCCCTTCCGCGACTACGTGGACCGCTTCTTCAAGACCCT
GCGCGCCGAGCAGGCCACCCAGGACGTGAAGAACTGGATGACCGACACCCTGCTGGTGCAGAACGCCAACCCCGACTGCAAG
ACCATCCTGCGCGCCCTGGGCCCCGGCGCCACCCTGGAGGAGATGATGACCGCCTGCCAGGGCGTGGGCGGCCCCTCCCACA

AGGCCCGCGTGCTGGCCGAGGCCATGTCCCAGGCCAACAACACCAACATCATGATGCAGCGCTCCAACTTCAAGGGCCCCAA
GCGCATCGTGAAGTGCTTCAACTGCGGCAAGGAGGGCCACATCGCCCGCAACTGCCGCGCCCCCCCGCAAGAAGGGCTGCTGG
AAGTGCGGCAAGGAGGGCCACCAGATGAAGGACTGCACCGAGCGCCAGGCCAACTTCCTGGGCAAGATCTGGCCCTCCCACA
AGGGCCGCCCCGGCAACTTCCTGCAGAACCGCCCCGAGCCCACCGCCCCCCCCCGCCGAGTCCTTCCGCTTCGAGGAGACCAC
CCCCGCCCCCAAGCAGGAGCCCAAGGACCGCGAGCCCCTGACCTCCCTGAAGTCCCTGTTCGGCTCCGACCCCCTGTCCCAG
TAA

9. 2003_C.anc.gag.PEP

MGARASILRGGKLDTWEKIRLRPGGKKHYMIKHLVWASRELERFALNPGLLETSEGCKQIMKQLQPALQTGTEELRSLYNTV
ATLYCVHERIEVRDTKEALDKIEEEQNKSQQKTQQAEAADGDNGKVSQNYPIVQNLQGQMVHQAISPRTLNAWVKVVEEKAF
SPEVIPMFTALSEGATPQDLNTMLNTVGGHQAAMQMLKDTINEEAAEWDRLHPVHAGPVAPGQMREPRGSDIAGTTSTLQEQ
IAWMTSNPPIPVGDIYKRWIILGLNKIVRMYSPVSILDIKQGPKEPFRDYVDRFFKTLRAEQATQDVKNWMTDTLLVQNANP
DCKTILRALGPGATLEEMMTACQGVGGPGHKARVLAEAMSQANNTNIMMQRSNFKGPKRIVKCFNCGKEGHIARNCRAPRKK
GCWKCGKEGHQMKDCTERQANFLGKIWPSHKGRPGNFLQSRPEPTAPPAESFRFEETTPAPKQEPKDREPLTSLKSLFGSDP
LSQ$

2003_C.anc.gag.OPT

ATGGGCGCCCGCGCCTCCATCCTGCGCGGCGGCAAGCTGGACACCTGGGAGAAGATCCGCCTGCGCCCCGGCGGCAAGAAGC
ACTACATGATCAAGCACCTGGTGTGGGCCTCCCGCGAGCTGGAGCGCTTCGCCCTGAACCCCGGCCTGCTGGAGACCTCCGA
GGGCTGCAAGCAGATCATGAAGCAGCTGCAGCCCGCCCTGCAGACCGGCACCGAGGAGCTGCGCTCCCTGTACAACACCGTG
GCCACCCTGTACTGCGTGCACGAGCGCATCGAGGTGCGCGACACCAAGGAGGCCCTGGACAAGATCGAGGAGGAGCAGAACA
AGTCCCAGCAGAAGACCCAGCAGGCCGAGGCCGCCGACGGCGACAACGGCAAGGTGTCCCAGAACTACCCCATCGTGCAGAA
CCTGCAGGGCCAGATGGTGCACCAGGCCATCTCCCCCCGCACCCTGAACGCCTGGGTGAAGGTGGTGGAGGAGAAGGCCTTC
TCCCCCGAGGTGATCCCCATGTTCACCGCCCTGTCCGAGGGCGCCACCCCCCAGGACCTGAACACCATGCTGAACACCGTGG
GCGGCCACCAGGCCGCCATGCAGATGCTGAAGGACACCATCAACGAGGAGGCCGCCGAGTGGGACCGCCTGCACCCCGTGCA
CGCCGGCCCCGTGGCCCCCGGCCAGATGCGCGAGCCCCGCGGCTCCGACATCGCCGGCACCACCTCCACCCTGCAGGAGCAG
ATCGCCTGGATGACCTCCAACCCCCCCATCCCCGTGGGCGACATCTACAAGCGCTGGATCATCCTGGGCCTGAACAAGATCG
TGCGCATGTACTCCCCCGTGTCCATCCTGGACATCAAGCAGGGCCCCAAGGAGCCCTTCCGCGACTACGTGGACCGCTTCTT
CAAGACCCTGCGCGCCGAGCAGGCCACCCAGGACGTGAAGAACTGGATGACCGACACCCTGCTGGTGCAGAACGCCAACCCC
GACTGCAAGACCATCCTGCGCGCCCTGGGCCCCGGCGCCACCCTGGAGGAGATGATGACCGCCTGCCAGGGCGTGGGCGGCC
CCGGCCACAAGGCCCGCGTGCTGGCCGAGGCCATGTCCCAGGCCAACAACACCAACATCATGATGCAGCGCTCCAACTTCAA
GGGCCCCAAGCGCATCGTGAAGTGCTTCAACTGCGGCAAGGAGGGCCACATCGCCCGCAACTGCCGCGCCCCCCGCAAGAAG
GGCTGCTGGAAGTGCGGCAAGGAGGGCCACCAGATGAAGGACTGCACCGAGCGCCAGGCCAACTTCCTGGGCAAGATCTGGC
CCTCCCACAAGGGCCGCCCCGGCAACTTCCTGCAGTCCCGCCCCGAGCCCACCGCCCCCCCCGCCGAGTCCTTCCGCTTCGA
GGAGACCACCCCCGCCCCCAAGCAGGAGCCCAAGGACCGCGAGCCCCTGACCTCCCTGAAGTCCCTGTTCGGCTCCGACCCC
CTGTCCCAGTAA

Fig. 6 C

10. 2003_CON_D gag.PEP

MGARASVLSGGKLDAWEKIRLRPGGKKKYRLKHIVWASRELERFALNPGLLETSEGCKQIIGQLQPAIQTGSEELRSLYNTV
ATLYCVHERIEVKDTKEALEKIEEEQNKSKKKAQQAAADTGNSSQVSQNYPIVQNLQGQMVHQAISPRTLNAWVKVIEEKAF
SPEVIPMFSALSEGATPQDLNTMLNTVGGHQAAMQMLKETINEEAAEWDRLHPVHAGPVAPGQMREPRGSDIAGTTSTLQEQ
IGWMTSNPPIPVGEIYKRWIILGLNKIVRMYSPVSILDIRQGPKEPFRDYVDRFYKTLRAEQASQDVKNWMTETLLVQNANP
DCKTILKALGPEATLEEMMTACQGVGGPSHKARVLAEAMSQATNSAAVMMQRGNFKGPRKIIKCFNCGKEGHIAKNCRAPRK
KGCWKCGKEGHQMKDCTERQANFLGKIWPSHKGRPGNFLQSRPEPTAPPAESFGFGEEITPSQKQEQKDKELYPLTSLKSLF
GNDPLSQ$

2003_CON_D gag.OPT

ATGGGCGCCCGCGCCTCCGTGCTGTCCGGCGGCAAGCTGGACGCCTGGGAGAAGATCCGCCTGCGCCCCGGCGGCAAGAAGA
AGTACCGCCTGAAGCACATCGTGTGGGCCTCCCGCGAGCTGGAGCGCTTCGCCCTGAACCCCGGCCTGCTGGAGACCTCCGA
GGGCTGCAAGCAGATCATCGGCCAGCTGCAGCCCGCCATCCAGACCGGCTCCGAGGAGCTGCGCTCCCTGTACAACACCGTG
GCCACCCTGTACTGCGTGCACGAGCGCATCGAGGTGAAGGACACCAAGGAGGCCCTGGAGAAGATCGAGGAGGAGCAGAACA
AGTCCAAGAAGAAGGCCCAGCAGGCCGCCGCCGACACCGGCAACTCCTCCCAGGTGTCCCAGAACTACCCCATCGTGCAGAA
CCTGCAGGGCCAGATGGTGCACCAGGCCATCTCCCCCCGCACCCTGAACGCCTGGGTGAAGGTGATCGAGGAGAAGGCCTTC
TCCCCCGAGGTGATCCCCATGTTCTCCGCCCTGTCCGAGGGCGCCACCCCCCAGGACCTGAACACCATGCTGAACACCGTGG
GCGGCCACCAGGCCGCCATGCAGATGCTGAAGGAGACCATCAACGAGGAGGCCGCCGAGTGGGACCGCCTGCACCCCGTGCA
CGCCGGCCCCGTGGCCCCCGGCCAGATGCGCGAGCCCCGCGGCTCCGACATCGCCGGCACCACCTCCACCCTGCAGGAGCAG
ATCGGCTGGATGACCTCCAACCCCCCCATCCCCGTGGGCGAGATCTACAAGCGCTGGATCATCCTGGGCCTGAACAAGATCG
TGCGCATGTACTCCCCCGTGTCCATCCTGGACATCCGCCAGGGCCCCAAGGAGCCCTTCCGCGACTACGTGGACCGCTTCTA
CAAGACCCTGCGCGCCGAGCAGGCCTCCCAGGACGTGAAGAACTGGATGACCGAGACCCTGCTGGTGCAGAACGCCAACCCC

Fig. 6 A

Fig. 6 B

GACTGCAAGACCATCCTGAAGGCCCTGGGCCCCGAGGCCACCCTGGAGGAGATGATGACCGCCTGCCAGGGCGTGGGCGGCC
CCTCCCACAAGGCCCGCGTGCTGGCCGAGGCCATGTCCCAGGCCACCAACTCCGCCGCCGTGATGATGCAGCGCGGCAACTT
CAAGGGCCCCCGCAAGATCATCAAGTGCTTCAACTGCGGCAAGGAGGGCCACATCGCCAAGAACTGCCGCGCCCCCCGCAAG
AAGGGCTGCTGGAAGTGCGGCAAGGAGGGCCACCAGATGAAGGACTGCACCGAGCGCCAGGCCAACTTCCTGGGCAAGATCT
GGCCCTCCCACAAGGGCCGCCCCGGCAACTTCCTGCAGTCCCGCCCCGAGCCCACCGCCCCCCCCGCCGAGTCCTTCGGCTT
CGGCGAGGAGATCACCCCCTCCCAGAAGCAGGAGCAGAAGGACAAGGAGCTGTACCCCCTGACCTCCCTGAAGTCCCTGTTC
GGCAACGACCCCCTGTCCCAGTAA

ig. 70

11. 2003_CON_F gag.PEP

A

MGARASVLSGGKLDAWEKIRLRPGGKKKYRMKHLVWASRELERFALDPGLLETSEGCQKIIGQLQPSLQTGSEELRSLYNTV
AVLYCVHQKVEVKDTKEALEKLEEEQNKSQQKTQQAAADKGVSQNYPIVQNLQGQMVHQAISPRTLNAWVKVIEEKAFSPEV
IPMFSALSEGATPQDLNTMLNTVGGHQAAMQMLKDTINEEAAEWDRLHPVHAGPIPPGQMREPRGSDIAGTTSTLQEQIQWM
TSNPPVPVGDIYKRWIILGLNKIVRMYSPVSILDIRQGPKEPFRDYVDRFFKTLRAEQATQEVKGWMTDTLLVQNANPDCKT
ILKALGPGATLEEMMTACQGVGGPGHKARVLAEAMSQATNTAIMMQKSNFKGQRRIVKCFNCGKEGHIAKNCRAPRKKGCWK
CGREGHQMKDCTERQANFLGKIWPSNKGRPGNFLQSRPEPTAPPAESFGFREEITPSPKQEQKDEGLYPPLASLKSLFGNDP
$

2003_CON_F gag.OPT

B

ATGGGCGCCCGCGCCTCCGTGCTGTCCGGCGGCAAGCTGGACGCCTGGGAGAAGATCCGCCTGCGCCCCGGCGGCAAGAAGA
AGTACCGCATGAAGCACCTGGTGTGGGCCTCCCGCGAGCTGGAGCGCTTCGCCCTGGACCCCGGCCTGCTGGAGACCTCCGA
GGGCTGCCAGAAGATCATCGGCCAGCTGCAGCCCTCCCTGCAGACCGGCTCCGAGGAGCTGCGCTCCCTGTACAACACCGTG
GCCGTGCTGTACTGCGTGCACCAGAAGGTGGAGGTGAAGGACACCAAGGAGGCCCTGGAGAAGCTGGAGGAGGAGCAGAACA
AGTCCCAGCAGAAGACCCAGCAGGCCGCCGCCGACAAGGGCGTGTCCCAGAACTACCCCATCGTGCAGAACCTGCAGGGCCA
GATGGTGCACCAGGCCATCTCCCCCCGCACCCTGAACGCCTGGGTGAAGGTGATCGAGGAGAAGGCCTTCTCCCCCGAGGTG
ATCCCCATGTTCTCCGCCCTGTCCGAGGGCGCCACCCCCCAGGACCTGAACACCATGCTGAACACCGTGGGCGGCCACCAGG
CCGCCATGCAGATGCTGAAGGACACCATCAACGAGGAGGCCGCCGAGTGGGACCGCCTGCACCCCGTGCACGCCGGCCCCAT
CCCCCCCGGCCAGATGCGCGAGCCCCGCGGCTCCGACATCGCCGGCACCACCTCCACCCTGCAGGAGCAGATCCAGTGGATG
ACCTCCAACCCCCCCCGTGCCCGTGGGCGACATCTACAAGCGCTGGATCATCCTGGGCCTGAACAAGATCGTGCGCATGTACT
CCCCCGTGTCCATCCTGGACATCCGCCAGGGCCCCAAGGAGCCCTTCCGCGACTACGTGGACCGCTTCTTCAAGACCCTGCG
CGCCGAGCAGGCCACCCAGGAGGTGAAGGGCTGGATGACCGACACCCTGCTGGTGCAGAACGCCAACCCCGACTGCAAGACC
ATCCTGAAGGCCCTGGGCCCCGGCGCCACCCTGGAGGAGATGATGACCGCCTGCCAGGGCGTGGGCGGCCCCGGCCACAAGG
CCCGCGTGCTGGCCGAGGCCATGTCCCAGGCCACCAACACCGCCATCATGATGCAGAAGTCCAACTTCAAGGGCCAGCGCCG
CATCGTGAAGTGCTTCAACTGCGGCAAGGAGGGCCACATCGCCAAGAACTGCCGCGCCCCCCGCAAGAAGGGCTGCTGGAAG
TGCGGCCGCGAGGGCCACCAGATGAAGGACTGCACCGAGCGCCAGGCCAACTTCCTGGGCAAGATCTGGCCCTCCAACAAGG
GCCGCCCCGGCAACTTCCTGCAGTCCCGCCCCGAGCCCACCGCCCCCCCCCGCCGAGTCCTTCGGCTTCCGCGAGGAGATCAC
CCCCTCCCCCAAGCAGGAGCAGAAGGACGAGGGCCTGTACCCCCCCCCTGGCCTCCCTGAAGTCCCTGTTCGGCAACGACCCC
TAA

ig. 71

12. 2003_CON_G gag.PEP

A

MGARASVLSGGKLDAWEKIRLRPGGKKKYRMKHLVWASRELERFALNPDLLETAEGCQQIMGQLQPALQTGTEELRSLFNTV
ATLYCVHQRIEVKDTKEALEEVEKIQKKSQQKTQQAAMDEGNSSQVSQNYPIVQNAQGQMVHQAISPRTLNAWVKVVEEKAF
SPEVIPMFSALSEGATPQDLNTMLNTVGGHQAAMQMLKDTINEEAAEWDRMHPQQAGPIPPGQIREPRGSDIAGTTSTLQEQ
IRWMTSNPPIPVGEIYKRWIILGLNKIVRMYSPVSILDIRQGPKEPFRDYVDRFFKTLRAEQATQEVKGWMTDTLLVQNANP
DCKTILRALGPGATLEEMMTACQGVGGPSHKARVLAEAMSQASGAAAAIMMQKSNFKGPRRTIKCFNCGKEGHLARNCRAPR
KKGCWKCGKEGHQMKDCTERQANFLGKIWPSNKGRPGNFLQNRPEPTAPPAESFGFGEEIAPSPKQEQKEKELYPLASLKSL
FGSDP$

2003_CON_G gag.OPT

B

ATGGGCGCCCGCGCCTCCGTGCTGTCCGGCGGCAAGCTGGACGCCTGGGAGAAGATCCGCCTGCGCCCCGGCGGCAAGAAGA
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GGGCTGCCAGCAGATCATGGGCCAGCTGCAGCCCGCCCTGCAGACCGGCACCGAGGAGCTGCGCTCCCTGTTCAACACCGTG
GCCACCCTGTACTGCGTGCACCAGCGCATCGAGGTGAAGGACACCAAGGAGGCCCTGGAGGAGGTGGAGAAGATCCAGAAGA
AGTCCCAGCAGAAGACCCAGCAGGCCGCCATGGACGAGGGCAACTCCTCCCAGGTGTCCCAGAACTACCCCATCGTGCAGAA
CGCCCAGGGCCAGATGGTGCACCAGGCCATCTCCCCCCGCACCCTGAACGCCTGGGTGAAGGTGGTGGAGGAGAAGGCCTTC
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ATCCGCTGGATGACCTCCAACCCCCCCCATCCCCGTGGGCGAGATCTACAAGCGCTGGATCATCCTGGGCCTGAACAAGATCG
TGCGCATGTACTCCCCCGTGTCCATCCTGGACATCCGCCAGGGCCCCAAGGAGCCCTTCCGCGACTACGTGGACCGCTTCTT

CAAGACCCTGCGCGCCGAGCAGGCCACCCAGGAGGTGAAGGGCTGGATGACCGACACCCTGCTGGTGCAGAACGCCAACCCC
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CCTCCCACAAGGCCCGCGTGCTGGCCGAGGCCATGTCCCAGGCCTCCGGCGCCGCCGCCGCCATCATGATGCAGAAGTCCAA
CTTCAAGGGCCCCCGCCGCACCATCAAGTGCTTCAACTGCGGCAAGGAGGGCCACCTGGCCCGCAACTGCCGCGCCCCCCGC
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TTCGGCTCCGACCCCTAA

13. 2003_CON_H gag.PEP

MGARASVLSGGKLDAWEKIRLRPGGKKKYRLKHLVWASRELERFALNPGLLETAEGCLQIIEQLQPAIKTGTEELQSLFNTV
AVLYCVHQRIDVKDTKEALGKIEEIQNKSQQKTQQAAADKEKDNKVSQNYPIVQNAQGQMVHQAISPRTLNAWVKVVEEKAF
SPEVIPMFSALSEGATPQDLNAMLNTVGGHQAAMQMLKDTINEEAAEWDRLHPVHAGPIPPGQMREPRGSDIAGTTSTLQEQ
IAWMTGNPPIPVGDIYKRWIILGLNKIVRMYSPVSILDIKQGPKEPFRDYVDRFFKTLRAEQATQDVKNWMTDTLLVQNANP
DCKTILRALGQGASIEEMMTACQGVGGPSHKARVLAEAMSQVTNANAAIMMQKGNFKGPRKIVKCFNCGKEGHIARNCRAPR
KKGCWKCGREGHQMKDCTERQANFLGKIWPSSKGRPGNFLQSRPEPTAPPAESFGFGEEMTPSPKQELKDKEPPLASLRSLF
GNDPLSQ$

2003_CON_H gag.OPT

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TGCGCATGTACTCCCCCGTGTCCATCCTGGACATCAAGCAGGGCCCCAAGGAGCCCTTCCGCGACTACGTGGACCGCTTCTT
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CCTCCCACAAGGCCCGCGTGCTGGCCGAGGCCATGTCCCAGGTGACCAACGCCAACGCCGCCATCATGATGCAGAAGGGCAA
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GGCAACGACCCCCTGTCCCAGTAA

14. 2003_CON_K gag.PEP

MGARASVLSGGKLDTWEKIRLRPGGKKKYRLKHLVWASRELERFALNPSLLETTEGCRQIIRQLQPSLQTGSEELKSLFNTV
ATLYCVHQRIEVRDTKEALDKLEEEQNKSQQKTQQETADKGVSQNYPIVQNLQGQMVHQALSPRTLNAWVKVIEEKAFSPEV
IPMFSALSEGATPQDLNTMLNTVGGHQAAMQMLKDTINEEAAEWDRLHPVHAGPIPPGQMREPRGSDIAGTTSTLQEQITWM
TSNPPVPVGEIYKRWIILGLNKIVRMYSPVSILDIRQGPKEPFRDYVDRFFKTLRAEQATQEVKNWMTDTLLVQNANPDCKT
ILKALGPGASLEEMMTACQGVGGPGHKARILAEAMSQVTNTAVMMQRGNFKGQRKIIKCFNCGKEGHIARNCRAPRKKGCWK
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LSQ$

2003_CON_K gag.OPT

ATGGGCGCCCGCGCCTCCGTGCTGTCCGGCGGCAAGCTGGACACCTGGGAGAAGATCCGCCTGCGCCCCGGCGGCAAGAAGA
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GCCACCCTGTACTGCGTGCACCAGCGCATCGAGGTGCGCGACACCAAGGAGGCCCTGGACAAGCTGGAGGAGGAGCAGAACA
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GATGGTGCACCAGGCCCTGTCCCCCCGCACCCTGAACGCCTGGGTGAAGGTGATCGAGGAGAAGGCCTTCTCCCCCGAGGTG
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CCGCCATGCAGATGCTGAAGGACACCATCAACGAGGAGGCCGCCGAGTGGGACCGCCTGCACCCCGTGCACGCCGGCCCCAT
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CCCCCGTGTCCATCCTGGACATCCGCCAGGGCCCCAAGGAGCCCTTCCGCGACTACGTGGACCGCTTCTTCAAGACCCTGCG
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CTGTCCCAGTAA

9.74

15. 2003_CON_01_AE gag.PEP

A

MGARASVLSGGKLDAWEKIRLRPGGKKKYRMKHLVWASRELERFALNPGLLETAEGCQQIIEQLQSTLKTGSEELKSLFNTV
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NPEVIPMFSALSEGATPQDLNMMLNIVGGHQAAMQMLKETINEEAAEWDRVHPVHAGPIPPGQMREPRGSDIAGTTSTLQEQ
IGWMTNNPPIPVGDIYKRWIILGLNKIVRMYSPVSILDIRQGPKEPFRDYVDRFYKTLRAEQATQEVKNWMTETLLVQNANP
DCKSILKALGTGATLEEMMTACQGVGGPSHKARVLAEAMSQAQHANIMMQRGNFKGQKRIKCFNCGKEGHLARNCRAPRKKG
CWKCGKEGHQMKDCTERQANFLGKIWPSNKGRPGNFPQSRPEPTAPPAENWGMGEEITSLPKQEQKDKEHPPPLVSLKSLFG
NDPLSQ$

2003_CON_01_AE gag.OPT

B

ATGGGCGCCCGCGCCTCCGTGCTGTCCGGCGGCAAGCTGGACGCCTGGGAGAAGATCCGCCTGCGCCCCGGCGGCAAGAAGA
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GGGCTGCCAGCAGATCATCGAGCAGCTGCAGTCCACCCTGAAGACCGGCTCCGAGGAGCTGAAGTCCCTGTTCAACACCGTG
GCCACCCTGTGGTGCGTGCACCAGCGCATCGAGGTGAAGGACACCAAGGAGGCCCTGGACAAGATCGAGGAGGTGCAGAACA
AGTCCCAGCAGAAGACCCAGCAGGCCGCCGCCGGCACCGGCTCCTCCTCCAAGGTGTCCCAGAACTACCCCATCGTGCAGAA
CGCCCAGGGCCAGATGGTGCACCAGCCCCTGTCCCCCCGCACCCTGAACGCCTGGGTGAAGGTGGTGGAGGAGAAGGGCTTC
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GCGGCCACCAGGCCGCCATGCAGATGCTGAAGGAGACCATCAACGAGGAGGCCGCCGAGTGGGACCGCGTGCACCCCGTGCA
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CCTCCCACAAGGCCCGCGTGCTGGCCGAGGCCATGTCCCAGGCCCAGCACGCCAACATCATGATGCAGCGCGGCAACTTCAA
GGGCCAGAAGCGCATCAAGTGCTTCAACTGCGGCAAGGAGGGCCACCTGGCCCGCAACTGCCGCGCCCCCCGCAAGAAGGGC
TGCTGGAAGTGCGGCAAGGAGGGCCACCAGATGAAGGACTGCACCGAGCGCCAGGCCAACTTCCTGGGCAAGATCTGGCCCT
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9.75

16. 2003_CON_02_AG gag.PEP

A

MGARASVLSGGKLDAWEKIRLRPGGKKKYRLKHLVWASRELERFALNPGLLETAEGCQQIMEQLQSALRTGSEELKSLYNTV
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VIPMFSALSEGATPQDLNMMLNIVGGHQAAMQMLKDTINEEAAEWDRVHPVHAGPIPPGQMREPRGSDIAGTTSTLQEQIGW
MTSNPPIPVGEIYKRWIVLGLNKIVRMYSPVSILDIRQGPKEPFRDYVDRFFKTLRAEQATQEVKNWMTETLLVQNANPDCK
SILRALGPGATLEEMMTACQGVGGPGHKARVLAEAMSQVQQSNIMMQRGNFRGQRTIKCFNCGKEGHLARNCKAPRKKGCWK
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2003_CON_02_AG gag.OPT

B

ATGGGCGCCCGCGCCTCCGTGCTGTCCGGCGGCAAGCTGGACGCCTGGGAGAAGATCCGCCTGCGCCCCGGCGGCAAGAAGA
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GGGCTGCCAGCAGATCATGGAGCAGCTGCAGTCCGCCCTGCGCACCGGCTCCGAGGAGCTGAAGTCCCTGTACAACACCGTG
GCCACCCTGTGGTGCGTGCACCAGCGCATCGACATCAAGGACACCAAGGAGGCCCTGGACAAGATCGAGGAGGTGCAGAACA
AGTCCAAGCAGAAGACCCAGCAGGCCGCCGCCGCCACCGGCTCCTCCTCCCAGAACTACCCCATCGTGCAGAACGCCCAGGG
CCAGATGACCCACCAGTCCATGTCCCCCCGCACCCTGAACGCCTGGGTGAAGGTGATCGAGGAGAAGGCCTTCTCCCCCGAG
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AGGCCGCCATGCAGATGCTGAAGGACACCATCAACGAGGAGGCCGCCGAGTGGGACCGCGTGCACCCCGTGCACGCCGGCCC
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GCGCGCCGAGCAGGCCACCCAGGAGGTGAAGAACTGGATGACCGAGACCCTGCTGGTGCAGAACGCCAACCCCGACTGCAAG
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AGGCCCGCGTGCTGGCCGAGGCCATGTCCCAGGTGCAGCAGTCCAACATCATGATGCAGCGCGGCAACTTCCGCGGCCAGCG
CACCATCAAGTGCTTCAACTGCGGCAAGGAGGGCCACCTGGCCCGCAACTGCAAGGCCCCCCGCAAGAAGGGCTGCTGGAAG
TGCGGCAAGGAGGGCCACCAGATGAAGGACTGCACCGAGCGCCAGGCCAACTTCCTGGGCAAGATCTGGCCCTCCTCCAAGG
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TAA

g.76

17. 2003_CON_03_ABG gag.PEP

A

MGARASVLSGGKLDAWEKIRLRPGGKKKYRIKHLVWASRELERFALNPSLLETSEGCQQILEQLQPTLKTGSEELKSLYNTV
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SPEVIPMFSALSEGATPQDLNMMLNIVGGHQAAMQMLKDTINEEAAEWDRLHPAQAGPFPPGQMREPRGSDIAGTTSTLQEQ
IGWMTSNPPIPVGDIYKRWIILGLNKIVRMYSPVSILDIRQGPKEPFRDYVDRFFKTLRAEQATQDVKNWMTETLLVQNANP
DCKTILRALGSGATLEEMMTACQGVGGPGHKARVLAEAMSQVQNANIMMQKSNFRGPKRIKCFNCGKDGHLARNCRAPRKKG
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NDPLSQ$

2003_CON_03_ABG gag.OPT

B

ATGGGCGCCCGCGCCTCCGTGCTGTCCGGCGGCAAGCTGGACGCCTGGGAGAAGATCCGCCTGCGCCCCGGCGGCAAGAAGA
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GGGCTGCCAGCAGATCCTGGAGCAGCTGCAGCCCACCCTGAAGACCGGCTCCGAGGAGCTGAAGTCCCTGTACAACACCGTG
GCCACCCTGTACTGCGTGCACCAGCGCATCGAGATCAAGGACACCAAGGAGGCCCTGGACAAGATCGAGGAGATCCAGAACA
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CGCCCAGGGCCAGATGACCCACCAGTCCATGTCCCCCCGCACCCTGAACGCCTGGGTGAAGGTGATCGAGGAGAAGGCCTTC
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TGCTGGAAGTGCGGCAAGGAGGGCCACCAGATGAAGGACTGCACCGAGCGCCAGGCCAACTTCCTGGGCCGCATCTGGCCCT
CCTCCAAGGGCCGCCCCGGCAACTTCCCCCAGTCCCGCCCCGAGCCCTCCGCCCCCCCCGCCGAGAACTTCGGCATGGGCGA
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AACGACCCCCTGTCCCAGTAA

ig.77

18. 2003_CON_04_CFX gag.PEP

A

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IGWMTSNPPIPVGEIYKRWIILGLNKIVRMYSPVSILDIRQGPKEPFRDYVDRFFKCLRAEQATQEVKNWMTETLLVQNANP
DCKSILKALGTGATLEEMMTACQGVGGPSHKARVLAEAMSQASNAAAAIMMQKSNFKGQRRIIKCFNCGKEGHLARNCRAPR
KKGCWKCGKEGHQMKDCTERQANFLGRMWPSSKGRPGNFLQSRPEPTAPPAESLEMKEETTSSPKQEPRDKELYPLTSLKSL
FGSDPLSQ$

2003 CON_04_CFX gag.OPT

B

ATGGGCGCCCGCGCCTCCGTGCTGTCCGGCGGCAAGCTGGACGCCTGGGAGCGCATCCGCCTGCGCCCCGGCGGCAAGAAGA
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CGCCCAGGGCCAGATGGTGCACCAGTCCATCTCCCCCCGCACCCTGAACGCCTGGGTGAAGGTGATCGAGGAGAAGGCCTTC
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TGTGGCCCTCCTCCAAGGGCCGCCCCGGCAACTTCCTGCAGTCCCGCCCCGAGCCCACCGCCCCCCCCGCCGAGTCCCTGGA
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TTCGGCTCCGACCCCCTGTCCCAGTAA

9.78

19. 2003_CON_06_CPX gag.PEP

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SPEVIPMFSALSEGATPQDLNMMLNIVGGHQAAMQMLKDTINEEAAEWDRVHPVHAGPIPPGQMREPRGSDIAGTTSTLQEQ
IGWMTSNPPIPVGEIYKRWIILGLNKIVRMYSPVSILDIRQGPKEPFRDYVDRFFKTLRAEQATQEVKNWMTDTLLVQNANP
DCKTILKALGPGATLEEMMTACQGVGGPGHKARVLAEAMSQASGTEAAIMMQKSNFKGPKRSIKCFNCGKEGHLARNCRAPR
KKGCWKCGKEGHQMKDCTERQANFLGKIWPSNKGRPGNFLQNRPEPTAPPAESFGFGEETAPSPKQEPKEKELYPLASLKSL
FGNDP$

2003_CON_06_CPX gag.OPT

B

ATGGGCGCCCGCGCCTCCGTGCTGTCCGGCGGCAAGCTGGACGAGTGGGAGAAGATCCGCCTGCGCCCCGGCGGCAAGAAGA
AGTACCGCCTGAAGCACCTGGTGTGGGCCTCCCGCGAGCTGGAGCGCTTCGCCCTGAACCCCGGCCTGCTGGAGACCGCCGA
GGGCTGCCAGCAGATCATCGAGCAGCTGCAGTCCGCCCTGAAGACCGGCTCCGAGGAGCTGAAGTCCCTGTACAACACCGTG
GCCACCCTGTACTGCGTGCACCAGCGCATCAAGGTGACCGACACCAAGGAGGCCCTGGACAAGATCGAGGAGATCCAGAACA
AGTCCAAGCAGAAGGCCCAGCAGGCCGCCGCCGCCACCGGCAACTCCTCCAACCTGTCCCAGAACTACCCCATCGTGCAGAA
CGCCCAGGGCCAGATGGTGCACCAGGCCATCTCCCCCCGCACCCTGAACGCCTGGGTGAAGGTGATCGAGGAGAAGGCCTTC
TCCCCCGAGGTGATCCCCATGTTCTCCGCCCTGTCCGAGGGCGCCACCCCCCAGGACCTGAACATGATGCTGAACATCGTGG
GCGGCCACCAGGCCGCCATGCAGATGCTGAAGGACACCATCAACGAGGAGGCCGCCGAGTGGGACCGCGTGCACCCCGTGCA
CGCCGGCCCCATCCCCCCCCGGCCAGATGCGCGAGCCCCGCGGCTCCGACATCGCCGGCACCACCTCCACCCTGCAGGAGCAG
ATCGGCTGGATGACCTCCAACCCCCCCATCCCCGTGGGCGAGATCTACAAGCGCTGGATCATCCTGGGCCTGAACAAGATCG
TGCGCATGTACTCCCCCGTGTCCATCCTGGACATCCGCCAGGGCCCCAAGGAGCCCTTCCGCGACTACGTGGACCGCTTCTT
CAAGACCCTGCGCGCCGAGCAGGCCACCCAGGAGGTGAAGAACTGGATGACCGACACCCTGCTGGTGCAGAACGCCAACCCC
GACTGCAAGACCATCCTGAAGGCCCTGGGCCCCGGCGCCACCCTGGAGGAGATGATGACCGCCTGCCAGGGCGTGGGCGGCC
CCGGCCACAAGGCCCGCGTGCTGGCCGAGGCCATGTCCCAGGCCTCCGGCACCGAGGCCGCCATCATGATGCAGAAGTCCAA
CTTCAAGGGCCCCAAGCGCTCCATCAAGTGCTTCAACTGCGGCAAGGAGGGCCACCTGGCCCGCAACTGCCGCGCCCCCCGC
AAGAAGGGCTGCTGGAAGTGCGGCAAGGAGGGCCACCAGATGAAGGACTGCACCGAGCGCCAGGCCAACTTCCTGGGCAAGA
TCTGGCCCTCCAACAAGGGCCGCCCCGGCAACTTCCTGCAGAACCGCCCCGAGCCCACCGCCCCCCCCGCCGAGTCCTTCGG
CTTCGGCGAGGAGACCGCCCCCTCCCCCAAGCAGGAGCCCAAGGAGAAGGAGCTGTACCCCCTGGCCTCCCTGAAGTCCCTG
TTCGGCAACGACCCCTAA

19.79

20. 2003_CON_07_BC gag.PEP

A

MGARASILRGGKLDKWEKIRLRPGGKKHYMLKHLVWASRELERFALNPGLLETSEGCKQIIKQLQPALQTGTEELRSLFNTV
ATLYCVHTEIDVRDTKEALDKIEEEQNKIQQKTQQAKEADGKVSQNYPIVQNLQGQMVHQPISPRTLNAWVKVVEEKAFSPE
VIPMFSALSEGATPQDLNTMLNTVGGHQAAMQILKDTINEEAAEWDRLHPVHAGPIAPGQMREPRGSDIAGTTSNLQEQIAW
MTSNPPVPVGDIYKRWIILGLNKIVRMYSPTSILDIKQGPKEPFRDYVDRFFKTLRAEQATQDVKNWMTDTLLVQNANPDCK
TILRALGPGASIEEMMTACQGVGGPSHKARVLAEAMSQTNSTILMQRSNFKGSKRIVKCFNCGKEGHIARNCRAPRKKGCWK
CGKEGHQMKDCTERQANFLGKIWPSHKGRPGNFLQSRPEPTAPPEESFRFGEETTTPSQKQEPIDKELYPLTSLKSLFGNDP
SSQ$

2003_CON_07_BC gag.OPT

B

ATGGGCGCCCGCGCCTCCATCCTGCGCGGCGGCAAGCTGGACAAGTGGGAGAAGATCCGCCTGCGCCCCGGCGGCAAGAAGC
ACTACATGCTGAAGCACCTGGTGTGGGCCTCCCGCGAGCTGGAGCGCTTCGCCCTGAACCCCGGCCTGCTGGAGACCTCCGA
GGGCTGCAAGCAGATCATCAAGCAGCTGCAGCCCGCCCTGCAGACCGGCACCGAGGAGCTGCGCTCCCTGTTCAACACCGTG
GCCACCCTGTACTGCGTGCACACCGAGATCGACGTGCGCGACACCAAGGAGGCCCTGGACAAGATCGAGGAGGAGCAGAACA
AGATCCAGCAGAAGACCCAGCAGGCCAAGGAGGCCGACGGCAAGGTGTCCCAGAACTACCCCATCGTGCAGAACCTGCAGGG
CCAGATGGTGCACCAGCCCATCTCCCCCCGCACCCTGAACGCCTGGGTGAAGGTGGTGGAGGAGAAGGCCTTCTCCCCCGAG
GTGATCCCCATGTTCTCCGCCCTGTCCGAGGGCGCCACCCCCCAGGACCTGAACACCATGCTGAACACCGTGGGCGGCCACC

AGGCCGCCATGCAGATCCTGAAGGACACCATCAACGAGGAGGCCGCCGAGTGGGACCGCCTGCACCCCGTGCACGCCGGCCC
CATCGCCCCCGGCCAGATGCGCGAGCCCCGCGGCTCCGACATCGCCGGCACCACCTCCAACCTGCAGGAGCAGATCGCCTGG
ATGACCTCCAACCCCCCCCGTGCCCGTGGGCGACATCTACAAGCGCTGGATCATCCTGGGCCTGAACAAGATCGTGCGCATGT
ACTCCCCCACCTCCATCCTGGACATCAAGCAGGGCCCCAAGGAGCCCTTCCGCGACTACGTGGACCGCTTCTTCAAGACCCT
GCGCGCCGAGCAGGCCACCCAGGACGTGAAGAACTGGATGACCGACACCCTGCTGGTGCAGAACGCCAACCCCGACTGCAAG
ACCATCCTGCGCGCCCTGGGCCCCGGCGCCTCCATCGAGGAGATGATGACCGCCTGCCAGGGCGTGGGCGGCCCCTCCCACA
AGGCCCGCGTGCTGGCCGAGGCCATGTCCCAGACCAACTCCACCATCCTGATGCAGCGCTCCAACTTCAAGGGCTCCAAGCG
CATCGTGAAGTGCTTCAACTGCGGCAAGGAGGGCCACATCGCCCGCAACTGCCGCGCCCCCCGCAAGAAGGGCTGCTGGAAG
TGCGGCAAGGAGGGCCACCAGATGAAGGACTGCACCGAGCGCCAGGCCAACTTCCTGGGCAAGATCTGGCCCTCCCACAAGG
GCCGCCCCGGCAACTTCCTGCAGTCCCGCCCCGAGCCCACCGCCCCCCCCGAGGAGTCCTTCCGCTTCGGCGAGGAGACCAC
CACCCCCTCCCAGAAGCAGGAGCCCATCGACAAGGAGCTGTACCCCCTGACCTCCCTGAAGTCCCTGTTCGGCAACGACCCC
TCCTCCCAGTAA

3.80A

21. 2003_CON_08_BC gag.PEP

MGARASILRGGKLDKWEKIRLRPGGKKHYMLKHLVWASRELERFALNPGLLETSEGCKQIIKQLQPALQTGTEELRSLFNTV
ATLYCVHAEIEVRDTKEALDKIEEEQNKIQQKTQQAKEADEKVSQNYPIVQNLQGQMVHQPLSPRTLNAWVKVVEEKAFSPE
VIPMFTALSEGATPQDLNTMLNTVGGHQAAMQMLKDTINEEAAEWDRLHPVHAGPVAPGQMREPRGSDIAGTTSTLQEQIGW
MTNNPPIPVGEIYKRWIILGLNKIVRMYSPTSILDIKQGPKEPFRDYVDRFFKTLRAEQATQDVKNWMTDTLLVQNANPDCK
TILRALGPGASLEEMMTACQGVGGPSHKARVLAEAMSQTNNTILMQRSNFKGSKRIVKCFNCGKEGHIAKNCRAPRKKGCWK
CGKEGHQMKDCTERQANFLGKIWPSHKGRPGNFLQSRPEPTAPPAESFRFEETTPAPKQEPKDREPLTSLRSLFGSDPLSQ$

2003_CON_08_BC gag.OPT

B

ATGGGCGCCCGCGCCTCCATCCTGCGCGGCGGCAAGCTGGACAAGTGGGAGAAGATCCGCCTGCGCCCCGGCGGCAAGAAGC
ACTACATGCTGAAGCACCTGGTGTGGGCCTCCCGCGAGCTGGAGCGCTTCGCCCTGAACCCCGGCCTGCTGGAGACCTCCGA
GGGCTGCAAGCAGATCATCAAGCAGCTGCAGCCCGCCCTGCAGACCGGCACCGAGGAGCTGCGCTCCCTGTTCAACACCGTG
GCCACCCTGTACTGCGTGCACGCCGAGATCGAGGTGCGCGACACCAAGGAGGCCCTGGACAAGATCGAGGAGGAGCAGAACA
AGATCCAGCAGAAGACCCAGCAGGCCAAGGAGGCCGACGAGAAGGTGTCCCAGAACTACCCCATCGTGCAGAACCTGCAGGG
CCAGATGGTGCACCAGCCCCTGTCCCCCCGCACCCTGAACGCCTGGGTGAAGGTGGTGGAGGAGAAGGCCTTCTCCCCCGAG
GTGATCCCCATGTTCACCGCCCTGTCCGAGGGCGCCACCCCCCAGGACCTGAACACCATGCTGAACACCGTGGGCGGCCACC
AGGCCGCCATGCAGATGCTGAAGGACACCATCAACGAGGAGGCCGCCGAGTGGGACCGCCTGCACCCCGTGCACGCCGGCCC
CGTGGCCCCCGGCCAGATGCGCGAGCCCCGCGGCTCCGACATCGCCGGCACCACCTCCACCCTGCAGGAGCAGATCGGCTGG
ATGACCAACAACCCCCCCCATCCCCGTGGGCGAGATCTACAAGCGCTGGATCATCCTGGGCCTGAACAAGATCGTGCGCATGT
ACTCCCCCACCTCCATCCTGGACATCAAGCAGGGCCCCAAGGAGCCCTTCCGCGACTACGTGGACCGCTTCTTCAAGACCCT
GCGCGCCGAGCAGGCCACCCAGGACGTGAAGAACTGGATGACCGACACCCTGCTGGTGCAGAACGCCAACCCCGACTGCAAG
ACCATCCTGCGCGCCCTGGGCCCCGGCGCCTCCCTGGAGGAGATGATGACCGCCTGCCAGGGCGTGGGCGGCCCCTCCCACA
AGGCCCGCGTGCTGGCCGAGGCCATGTCCCAGACCAACAACACCATCCTGATGCAGCGCTCCAACTTCAAGGGCTCCAAGCG
CATCGTGAAGTGCTTCAACTGCGGCAAGGAGGGCCACATCGCCAAGAACTGCCGCGCCCCCCGCAAGAAGGGCTGCTGGAAG
TGCGGCAAGGAGGGCCACCAGATGAAGGACTGCACCGAGCGCCAGGCCAACTTCCTGGGCAAGATCTGGCCCTCCCACAAGG
GCCGCCCCGGCAACTTCCTGCAGTCCCGCCCCGAGCCCACCGCCCCCCCCGCCGAGTCCTTCCGCTTCGAGGAGACCACCCC
CGCCCCCAAGCAGGAGCCCAAGGACCGCGAGCCCCTGACCTCCCTGCGCTCCCTGTTCGGCTCCGACCCCCTGTCCCAGTAA

3.81A

22. 2003_CON_10_CD gag.PEP

MGARASVLSGGKLDEWEKIRLRPGGKKKYRLKHLVWASRELERFALNPGLLETSEGCKQIIGQLQPAIQTGSEEIKSLYNTV
ATLYCVHERIKVTDTKEALDKIEEEQTKSKKKAQQATADTGNSSQVSQNYPIVQNLQGQMVHQPLSPRTLNAWVKVIEEKAF
SPEVIPMFSALSEGATPQDLNTMLNTVGGHQAAMQMLKETINEEAAEWDRLHPVQAGPVAPGQIREPRGSDIAGTTSTLQEQ
IRWMTSNPPIPVGEIYKRWIILGLNKIVRMYSPVSILDIRQGPKEPFRDYVDRFYKTLRAEQASQDVKNWMTETLLVQNANP
DCKTILKALGPAATLEEMMTACQGVGGPSHKARVLAEAMSQATSGNAIMMQRGNFKGPKKIIKCFNCGKEGHIAKNCRAPRK
KGCWKCGREGHQMKDCTERQANFLGKIWPSNKGRPGNFLQSRPEPTAPPAESFGFGEEITPSQKQEQKDKELHPLASLKSLF
GNDPLSQ$

2003_CON_10_CD gag.OPT

B

ATGGGCGCCCGCGCCTCCGTGCTGTCCGGCGGCAAGCTGGACGAGTGGGAGAAGATCCGCCTGCGCCCCGGCGGCAAGAAGA
AGTACCGCCTGAAGCACCTGGTGTGGGCCTCCCGCGAGCTGGAGCGCTTCGCCCTGAACCCCGGCCTGCTGGAGACCTCCGA
GGGCTGCAAGCAGATCATCGGCCAGCTGCAGCCCGCCATCCAGACCGGCTCCGAGGAGATCAAGTCCCTGTACAACACCGTG
GCCACCCTGTACTGCGTGCACGAGCGCATCAAGGTGACCGACACCAAGGAGGCCCTGGACAAGATCGAGGAGGAGCAGACCA
AGTCCAAGAAGAAGGCCCAGCAGGCCACCGCCGACACCGGCAACTCCTCCCAGGTGTCCCAGAACTACCCCATCGTGCAGAA
CCTGCAGGGCCAGATGGTGCACCAGCCCCTGTCCCCCCGCACCCTGAACGCCTGGGTGAAGGTGATCGAGGAGAAGGCCTTC
TCCCCCGAGGTGATCCCCATGTTCTCCGCCCTGTCCGAGGGCGCCACCCCCCAGGACCTGAACACCATGCTGAACACCGTGG
GCGGCCACCAGGCCGCCATGCAGATGCTGAAGGAGACCATCAACGAGGAGGCCGCCGAGTGGGACCGCCTGCACCCCGTGCA

GGCCGGCCCCGTGGCCCCCGGCCAGATCCGCGAGCCCCGCGGCTCCGACATCGCCGGCACCACCTCCACCCTGCAGGAGCAG
ATCCGCTGGATGACCTCCAACCCCCCCATCCCCGTGGGCGAGATCTACAAGCGCTGGATCATCCTGGGCCTGAACAAGATCG
TGCGCATGTACTCCCCCGTGTCCATCCTGGACATCCGCCAGGGCCCCAAGGAGCCCTTCCGCGACTACGTGGACCGCTTCTA
CAAGACCCTGCGCGCCGAGCAGGCCTCCCAGGACGTGAAGAACTGGATGACCGAGACCCTGCTGGTGCAGAACGCCAACCCC
GACTGCAAGACCATCCTGAAGGCCCTGGGCCCCGCCGCCACCCTGGAGGAGATGATGACCGCCTGCCAGGGCGTGGGCGGCC
CCTCCCACAAGGCCCGCGTGCTGGCCGAGGCCATGTCCCAGGCCACCTCCGGCAACGCCATCATGATGCAGCGCGGCAACTT
CAAGGGCCCCAAGAAGATCATCAAGTGCTTCAACTGCGGCAAGGAGGGCCACATCGCCAAGAACTGCCGCGCCCCCCGCAAG
AAGGGCTGCTGGAAGTGCGGCCGCGAGGGCCACCAGATGAAGGACTGCACCGAGCGCCAGGCCAACTTCCTGGGCAAGATCT
GGCCCTCCAACAAGGGCCGCCCCGGCAACTTCCTGCAGTCCCGCCCCGAGCCCACCGCCCCCCCCGCCGAGTCCTTCGGCTT
CGGCGAGGAGATCACCCCCTCCCAGAAGCAGGAGCAGAAGGACAAGGAGCTGCACCCCCTGGCCTCCCTGAAGTCCCTGTTC
GGCAACGACCCCCTGTCCCAGTAA

3.82

23. 2003_CON_11_CPX gag.PEP

A

gag.PEPMGARASVLSGGKLDAWEKIRLRPGGKKKYRLKHLVWASRELERFALNPSLLETAEGCQQIMGQLQPALGTGTEEL
RSLYNTVATLYCVHHRIEVKDTKEALDKIEEIQNKSKQKKQQAAADTGNSSKVSQNYPIVQNAQGQMVHQAISPRTLNAWVK
VVEEKAFSPEVIPMFSALSEGATPQDLNMMLNIVGGHQAAMQMLKDTINEEAAEWDRVHPVHAGPIPPGQMREPRGSDIAGT
TSTLQEQIGWMTGNPPVPVGEIYRRWIILGLNKIVRMYSPVSILDIRQGPKEPFRDYVDRFFKTLRAEQATQEVKSWMTETL
LIQNANPDCKSILRALGPGATLEEMMTACQGVGGPGHKARVLAEAMSQVQQTNIMMQRSNFKGQKRIKCFNCGKEGHLARNC
RAPRKKGCWKCGKEGHQMKDCTERQANFLGKIWPSSKGRPGNFLQSRPEPTAPPAESFGFGEEIAPSPKQEPKEKELYPLTS
LKSLFGSDPLSQ$

2003_CON_11_CPX gag.OPT

B

ATGGGCGCCCGCGCCTCCGTGCTGTCCGGCGGCAAGCTGGACGCCTGGGAGAAGATCCGCCTGCGCCCCGGCGGCAAGAAGA
AGTACCGCCTGAAGCACCTGGTGTGGGCCTCCCGCGAGCTGGAGCGCTTCGCCCTGAACCCCTCCCTGCTGGAGACCGCCGA
GGGCTGCCAGCAGATCATGGGCCAGCTGCAGCCCGCCCTGGGCACCGGCACCGAGGAGCTGCGCTCCCTGTACAACACCGTG
GCCACCCTGTACTGCGTGCACCACCGCATCGAGGTGAAGGACACCAAGGAGGCCCTGGACAAGATCGAGGAGATCCAGAACA
AGTCCAAGCAGAAGAAGCAGCAGGCCGCCGCCGACACCGGCAACTCCTCCAAGGTGTCCCAGAACTACCCCATCGTGCAGAA
CGCCCAGGGCCAGATGGTGCACCAGGCCATCTCCCCCCGCACCCTGAACGCCTGGGTGAAGGTGGTGGAGGAGAAGGCCTTC
TCCCCCGAGGTGATCCCCATGTTCTCCGCCCTGTCCGAGGGCGCCACCCCCCAGGACCTGAACATGATGCTGAACATCGTGG
GCGGCCACCAGGCCGCCATGCAGATGCTGAAGGACACCATCAACGAGGAGGCCGCCGAGTGGGACCGCGTGCACCCCGTGCA
CGCCGGCCCCATCCCCCCCGGCCAGATGCGCGAGCCCCGCGGCTCCGACATCGCCGGCACCACCTCCACCCTGCAGGAGCAG
ATCGGCTGGATGACCGGCAACCCCCCCGTGCCCGTGGGCGAGATCTACCGCCGCTGGATCATCCTGGGCCTGAACAAGATCG
TGCGCATGTACTCCCCCGTGTCCATCCTGGACATCCGCCAGGGCCCCAAGGAGCCCTTCCGCGACTACGTGGACCGCTTCTT
CAAGACCCTGCGCGCCGAGCAGGCCACCCAGGAGGTGAAGTCCTGGATGACCGAGACCCTGCTGATCCAGAACGCCAACCCC
GACTGCAAGTCCATCCTGCGCGCCCTGGGCCCCGGCGCCACCCTGGAGGAGATGATGACCGCCTGCCAGGGCGTGGGCGGCC
CCGGCCACAAGGCCCGCGTGCTGGCCGAGGCCATGTCCCAGGTGCAGCAGACCAACATCATGATGCAGCGCTCCAACTTCAA
GGGCCAGAAGCGCATCAAGTGCTTCAACTGCGGCAAGGAGGGCCACCTGGCCCGCAACTGCCGCGCCCCCCGCAAGAAGGGC
TGCTGGAAGTGCGGCAAGGAGGGCCACCAGATGAAGGACTGCACCGAGCGCCAGGCCAACTTCCTGGGCAAGATCTGGCCCT
CCTCCAAGGGCCGCCCCGGCAACTTCCTGCAGTCCCGCCCCGAGCCCACCGCCCCCCCCGCCGAGTCCTTCGGCTTCGGCGA
GGAGATCGCCCCCTCCCCCAAGCAGGAGCCCAAGGAGAAGGAGCTGTACCCCCTGACCTCCCTGAAGTCCCTGTTCGGCTCC
GACCCCCTGTCCCAGTAA

Fig. 83

24. 2003_CON_12_BF.gag.PEP

A

MGARASVLSGGELDRWEKIRLRPGGKKKYRLKHIVWASRELERFAVNPGLLETSEGCRKIIGQLQPSLQTGSEELRSLYNTI
AVLYFVHQKVEVKDTKEALDKLEEEQNKSQQKTQQAAADKGVSQNYPIVQNLQGQMVHQALSPRTLNAWVKVVEEKAFSPEV
IPMFSALSEGATPQDLNTMLNTVGGHQAAMQMLKDTINEEAAEWDRLHPVHAGPIPPGQMREPRGSDIAGTTSTLQEQIQWM
TSNPPVPVGEIYKRWIILGLNKIVRMYSPVSILDIRQGPKEPFRDYVDRFFKTLRAEQATQEVKGWMTDTLLVQNANPDCKT
ILKALGPGATLEEMMTACQGVGGPGHKARVLAEAMSQVTNTTVMMQKSNFKGQRRIVKCFNCGKEGHIAKNCRAPRKKGCWK
CGREGHQMKDCTERQANFLGKIWPSNKGRPGNFLQNRPEPTAPPAESFGFGEEITPSPKQEQKDEGLYPPLASLKSLFGNDP
$

2003_CON_12_BF.gag.OPT

B

ATGGGCGCCCGCGCCTCCGTGCTGTCCGGCGGCGAGCTGGACCGCTGGGAGAAGATCCGCCTGCGCCCCGGCGGCAAGAAGA
AGTACCGCCTGAAGCACATCGTGTGGGCCTCCCGCGAGCTGGAGCGCTTCGCCGTGAACCCCGGCCTGCTGGAGACCTCCGA
GGGCTGCCGCAAGATCATCGGCCAGCTGCAGCCCTCCCTGCAGACCGGCTCCGAGGAGCTGCGCTCCCTGTACAACACCATC
GCCGTGCTGTACTTCGTGCACCAGAAGGTGGAGGTGAAGGACACCAAGGAGGCCCTGGACAAGCTGGAGGAGGAGCAGAACA
AGTCCCAGCAGAAGACCCAGCAGGCCGCCGCCGACAAGGGCGTGTCCCAGAACTACCCCATCGTGCAGAACCTGCAGGGCCA
GATGGTGCACCAGGCCCTGTCCCCCCCGCACCCTGAACGCCTGGGTGAAGGTGGTGGAGGAGAAGGCCTTCTCCCCCGAGGTG
ATCCCCATGTTCTCCGCCCTGTCCGAGGGCGCCACCCCCCAGGACCTGAACACCATGCTGAACACCGTGGGCGGCCACCAGG

CCGCCATGCAGATGCTGAAGGACACCATCAACGAGGAGGCCGCCGAGTGGGACCGCCTGCACCCCGTGCACGCCGGCCCCAT
CCCCCCCGGCCAGATGCGCGAGCCCCGCGGCTCCGACATCGCCGGCACCACCTCCACCCTGCAGGAGCAGATCCAGTGGATG
ACCTCCAACCCCCCCGTGCCCGTGGGCGAGATCTACAAGCGCTGGATCATCCTGGGCCTGAACAAGATCGTGCGCATGTACT
CCCCCGTGTCCATCCTGGACATCCGCCAGGGCCCCAAGGAGCCCTTCCGCGACTACGTGGACCGCTTCTTCAAGACCCTGCG
CGCCGAGCAGGCCACCCAGGAGGTGAAGGGCTGGATGACCGACACCCTGCTGGTGCAGAACGCCAACCCCGACTGCAAGACC
ATCCTGAAGGCCCTGGGCCCCGGCGCCACCCTGGAGGAGATGATGACCGCCTGCCAGGGCGTGGGCGGCCCCGGCCACAAGG
CCCGCGTGCTGGCCGAGGCCATGTCCCAGGTGACCAACACCACCGTGATGATGCAGAAGTCCAACTTCAAGGGCCAGCGCCG
CATCGTGAAGTGCTTCAACTGCGGCAAGGAGGGCCACATCGCCAAGAACTGCCGCGCCCCCCGCAAGAAGGGCTGCTGGAAG
TGCGGCCGCGAGGGCCACCAGATGAAGGACTGCACCGAGCGCCAGGCCAACTTCCTGGGCAAGATCTGGCCCTCCAACAAGG
GCCGCCCCGGCAACTTCCTGCAGAACCGCCCCGAGCCCACCGCCCCCCCCGCCGAGTCCTTCGGCTTCGGCGAGGAGATCAC
CCCCTCCCCCAAGCAGGAGCAGAAGGACGAGGGCCTGTACCCCCCCCTGGCCTCCCTGAAGTCCCTGTTCGGCAACGACCCC
TAA

1,84 A

25. 2003_CON_14_BG gag.PEP

MGARASVLSGGKLDAWEKIRLRPGGKKKYRMKHLVWASRELERFALNPDLLETAEGCQQIMGQLQPALQTGTEEIRSLFNTV
ATLYCVHQKIEVKDTKEALEEVEKAQKKSQKKQQAAMDEGNNSQASQNYPIVQNAQGQMVHQAISPRTLNAWVKVVEEKAFS
PEVIPMFSALSEGATPQDLNIMLNTVGGHQAAMQMLKDTINEEAAEWDRMHPQQAGPIPPGQIREPRGSDIAGTTSTLQEQI
RWMTSNPPIPVGEIYKRWIILGLNKIVRMYSPVSILDIRQGPKEPFRDYVDRFFKTLRAEQATQEVKGWMTDTLLVQNANPD
CKTILRALGPGATLEEMMTACQGVGGPSHKARVLAEAMSQASGATIMMQKSNFKGPRRNIKCFNCGKEGHLARNCRAPRKKG
CWKCGKEGHQMKDCTESKANFLGKIWPSNKGRPGNFLQNRPEPTAPPAESFGFGEEIAPSPKQEPKEKEIYPLASLKSLFGS
DPSQ

B

2003_CON_14_BG gag.OPT

ATGGGCGCCCGCGCCTCCGTGCTGTCCGGCGGCAAGCTGGACGCCTGGGAGAAGATCCGCCTGCGCCCCGGCGGCAAGAAGA
AGTACCGCATGAAGCACCTGGTGTGGGCCTCCCGCGAGCTGGAGCGCTTCGCCCTGAACCCCGACCTGCTGGAGACCGCCGA
GGGCTGCCAGCAGATCATGGGCCAGCTGCAGCCCGCCCTGCAGACCGGCACCGAGGAGATCCGCTCCCTGTTCAACACCGTG
GCCACCCTGTACTGCGTGCACCAGAAGATCGAGGTGAAGGACACCAAGGAGGCCCTGGAGGAGGTGGAGAAGGCCCAGAAGA
AGTCCCAGAAGAAGCAGCAGGCCGCCATGGACGAGGGCAACAACTCCCAGGCCTCCCAGAACTACCCCATCGTGCAGAACGC
CCAGGGCCAGATGGTGCACCAGGCCATCTCCCCCCGCACCCTGAACGCCTGGGTGAAGGTGGTGGAGGAGAAGGCCTTCTCC
CCCGAGGTGATCCCCATGTTCTCCGCCCTGTCCGAGGGCGCCACCCCCCAGGACCTGAACACCATGCTGAACACCGTGGGCG
GCCACCAGGCCGCCATGCAGATGCTGAAGGACACCATCAACGAGGAGGCCGCCGAGTGGGACCGCATGCACCCCCAGCAGGC
CGGCCCCATCCCCCCCCGGCCAGATCCGCGAGCCCCGCGGCTCCGACATCGCCGGCACCACCTCCACCCTGCAGGAGCAGATC
CGCTGGATGACCTCCAACCCCCCCATCCCCGTGGGCGAGATCTACAAGCGCTGGATCATCCTGGGCCTGAACAAGATCGTGC
GCATGTACTCCCCCGTGTCCATCCTGGACATCCGCCAGGGCCCCAAGGAGCCCTTCCGCGACTACGTGGACCGCTTCTTCAA
GACCCTGCGCGCCGAGCAGGCCACCCAGGAGGTGAAGGGCTGGATGACCGACACCCTGCTGGTGCAGAACGCCAACCCCGAC
TGCAAGACCATCCTGCGCGCCCTGGGCCCCGGCGCCACCCTGGAGGAGATGATGACCGCCTGCCAGGGCGTGGGCGGCCCCT
CCCACAAGGCCCGCGTGCTGGCCGAGGCCATGTCCCAGGCCTCCGGCGCCACCATCATGATGCAGAAGTCCAACTTCAAGGG
CCCCCGCCGCAACATCAAGTGCTTCAACTGCGGCAAGGAGGGCCACCTGGCCCGCAACTGCCGCGCCCCCCGCAAGAAGGGC
TGCTGGAAGTGCGGCAAGGAGGGCCACCAGATGAAGGACTGCACCGAGTCCAAGGCCAACTTCCTGGGCAAGATCTGGCCCT
CCAACAAGGGCCGCCCCGGCAACTTCCTGCAGAACCGCCCCGAGCCCACCGCCCCCCCCGCCGAGTCCTTCGGCTTCGGCGA
GGAGATCGCCCCCTCCCCCAAGCAGGAGCCCAAGGAGAAGGAGATCTACCCCCTGGCCTCCCTGAAGTCCCTGTTCGGCTCC
GACCCCTAATCCCAGTAA

Fig. 85

A

31. 2003_CONS nef.PEP

MGGKWSKSSIVGWPAVRERIRRTPPAAEGVGAVSQDLDKHGAITSSNTAATNADCAWLEAQEEEEVGFPVRPQVPLRPMTYK
GAFDLSHFLKEKGGLDGLIYSKKRQEILDLWVYHTQGYFPDWQNYTPGPGIRYPLTFGWCFKLVPVDPEEVEEANEGENNCL
LHPMCQHGMEDEDREVLMWKFDSRLALRHIARELHPEFYKDC$

B

2003_CONS nef.OPT

ATGGGCGGCAAGTGGTCCAAGTCCTCCATCGTGGGCTGGCCCGCCGTGCGCGAGCGCATCCGCCGCACCCCCCCCGCCGCCG
AGGGCGTGGGCGCCGTGTCCCAGGACCTGGACAAGCACGGCGCCATCACCTCCTCCAACACCGCCGCCACCAACGCCGACTG
CGCCTGGCTGGAGGCCCAGGAGGAGGAGGAGGTGGGCTTCCCCGTGCGCCCCCAGGTGCCCCTGCGCCCCATGACCTACAAG
GGCGCCTTCGACCTGTCCCACTTCCTGAAGGAGAAGGGCGGCCTGGACGGCCTGATCTACTCCAAGAAGCGCCAGGAGATCC
TGGACCTGTGGGTGTACCACACCCAGGGCTACTTCCCCGACTGGCAGAACTACACCCCCGGCCCCGGCATCCGCTACCCCCT
GACCTTCGGCTGGTGCTTCAAGCTGGTGCCCGTGGACCCCGAGGAGGTGGAGGAGGCCAACGAGGGCGAGAACAACTGCCTG
CTGCACCCCATGTGCCAGCACGGCATGGAGGACGAGGACCGCGAGGTGCTGATGTGGAAGTTCGACTCCCGCCTGGCCCTGC
GCCACATCGCCCGCGAGCTGCACCCCGAGTTCTACAAGGACTGCTAA

Fig. 86

A

32. 2003_M. GROUP.anc nef.PEP

MGGKWSKSSIVGWPAVRERMRRTAPAAEGVGAVSQDLDKHGAITSSNTAATNADCAWLEAQEEEEVGFPVRPQVPLRPMTYK
AAFDLSHFLKEKGGLDGLIYSKKRQEILDLWVYHTQGYFPDWQNYTPGPGIRYPLTFGWCFKLVPVDPEEVEEANEGENNCL
LHPMCQHGMEDEEREVLMWKFDSRLALRHIARELHPEFYKDC$

B

2003_M GROUP.anc nef.OPT

ATGGGCGGCAAGTGGTCCAAGTCCTCCATCGTGGGCTGGCCCGCCGTGCGCGAGCGCATGCGCCGCACCGCCCCCGCCGCCG
AGGGCGTGGGCGCCGTGTCCCAGGACCTGGACAAGCACGGCGCCATCACCTCCTCCAACACCGCCGCCACCAACGCCGACTG
CGCCTGGCTGGAGGCCCAGGAGGAGGAGGAGGTGGGCTTCCCCGTGCGCCCCCAGGTGCCCCTGCGCCCCATGACCTACAAG
GCCGCCTTCGACCTGTCCCACTTCCTGAAGGAGAAGGGCGGCCTGGACGGCCTGATCTACTCCAAGAAGCGCCAGGAGATCC
TGGACCTGTGGGTGTACCACACCCAGGGCTACTTCCCCGACTGGCAGAACTACACCCCCGGCCCCGGCATCCGCTACCCCCT
GACCTTCGGCTGGTGCTTCAAGCTGGTGCCCGTGGACCCCGAGGAGGTGGAGGAGGCCAACGAGGGCGAGAACAACTGCCTG
CTGCACCCCATGTGCCAGCACGGCATGGAGGACGAGGAGCGCGAGGTGCTGATGTGGAAGTTCGACTCCCGCCTGGCCCTGC
GCCACATCGCCCGCGAGCTGCACCCCGAGTTCTACAAGGACTGCTAA

Fig. 87

A

33. 2003_CON_A nef.PEP

MGGKWSKSSIVGWPDIRERIRRTPPAAKGVGAVSQDLDKYGAVTINNTAATQASCAWLEAQEEEEEVGFPVRPQVPLRPMTF
KGAFDLSFFLKEKGGLDGLIYSQKRQEILDLWVYNTQGYFPDWQNYTPGPGTRFPLTFGWCFKLVPVDPDEVEEATEGENNC
LLHPICQHGMDDEEKEVLMWKFDSRLARRHIALEMHPEFYKDC$

B

2003_CON_A nef.OPT

ATGGGCGGCAAGTGGTCCAAGTCCTCCATCGTGGGCTGGCCCGACATCCGCGAGCGCATCCGCCGCACCCCCCCCGCCGCCA
AGGGCGTGGGCGCCGTGTCCCAGGACCTGGACAAGTACGGCGCCGTGACCATCAACAACACCGCCGCCACCCAGGCCTCCTG
CGCCTGGCTGGAGGCCCAGGAGGAGGAGGAGGAGGTGGGCTTCCCCGTGCGCCCCCAGGTGCCCCTGCGCCCCATGACCTTC
AAGGGCGCCTTCGACCTGTCCTTCTTCCTGAAGGAGAAGGGCGGCCTGGACGGCCTGATCTACTCCCAGAAGCGCCAGGAGA
TCCTGGACCTGTGGGTGTACAACACCCAGGGCTACTTCCCCGACTGGCAGAACTACACCCCCGGCCCCGGCACCCGCTTCCC
CCTGACCTTCGGCTGGTGCTTCAAGCTGGTGCCCGTGGACCCCGACGAGGTGGAGGAGGCCACCGAGGGCGAGAACAACTGC
CTGCTGCACCCCATCTGCCAGCACGGCATGGACGACGAGGAGAAGGAGGTGCTGATGTGGAAGTTCGACTCCCGCCTGGCCC
GCCGCCACATCGCCCTGGAGATGCACCCCGAGTTCTACAAGGACTGCTAA

Fig. 88

A

34. 2003_CON_A1 nef.PEP

MGGKWSKSSIVGWPEVRERMRRTPPAATGVGAVSQDLDKHGAVTSSNINHPSCVWLEAQEEEEVGFPVRPQVPLRPMTYKGA
LDLSHFLKEKGGLDGLIYSRKRQEILDLWVYHTQGYFPDWQNYTPGPGIRYPLTFGWCFKLVPVDPDEVEKATEGENNSLLH
PICQHGMDDEEREVLKWKFDSRLALKHRAQELHPEFYKDC$

B

2003_CON_A1 nef.OPT

ATGGGCGGCAAGTGGTCCAAGTCCTCCATCGTGGGCTGGCCCGAGGTGCGCGAGCGCATGCGCCGCACCCCCCCCGCCGCCA
CCGGCGTGGGCGCCGTGTCCCAGGACCTGGACAAGCACGGCGCCGTGACCTCCTCCAACATCAACCACCCCTCCTGCGTGTG
GCTGGAGGCCCAGGAGGAGGAGGAGGTGGGCTTCCCCGTGCGCCCCCAGGTGCCCCTGCGCCCCATGACCTACAAGGGCGCC
CTGGACCTGTCCCACTTCCTGAAGGAGAAGGGCGGCCTGGACGGCCTGATCTACTCCCGCAAGCGCCAGGAGATCCTGGACC
TGTGGGTGTACCACACCCAGGGCTACTTCCCCGACTGGCAGAACTACACCCCCGGCCCCGGCATCCGCTACCCCCTGACCTT
CGGCTGGTGCTTCAAGCTGGTGCCCGTGGACCCCGACGAGGTGGAGAAGGCCACCGAGGGCGAGAACAACTCCCTGCTGCAC
CCCATCTGCCAGCACGGCATGGACGACGAGGAGCGCGAGGTGCTGAAGTGGAAGTTCGACTCCCGCCTGGCCCTGAAGCACC
GCGCCCAGGAGCTGCACCCCGAGTTCTACAAGGACTGCTAA

C

35. 2003_A1.anc nef.PEP

MGGKWSKSSIVGWPEVRERMRRTPPAAKGVGAVSQDLDKHGAVTSSNTAANNPGCAWLEAQEEEEVGFPVRPQVPLRPMTYK
GAFDLSHFLKEKGGLDGLIYSKKRQEILDLWVYHTQGYFPDWQNYTPGPGIRYPLTFGWCFKLVPVDPAEVEEATEGENNSL
LHPICQHGMDDEEREVLMWKFDSRLALKHRARELHPEFYKDC$

D

2003_A1.anc nef.OPT

ATGGGCGGCAAGTGGTCCAAGTCCTCCATCGTGGGCTGGCCCGAGGTGCGCGAGCGCATGCGCCGCACCCCCCCCGCCGCCA
AGGGCGTGGGCGCCGTGTCCCAGGACCTGGACAAGCACGGCGCCGTGACCTCCTCCAACACCGCCGCCAACAACCCCGGCTG
CGCCTGGCTGGAGGCCCAGGAGGAGGAGGAGGTGGGCTTCCCCGTGCGCCCCCAGGTGCCCCTGCGCCCCATGACCTACAAG
GGCGCCTTCGACCTGTCCCACTTCCTGAAGGAGAAGGGCGGCCTGGACGGCCTGATCTACTCCAAGAAGCGCCAGGAGATCC
TGGACCTGTGGGTGTACCACACCCAGGGCTACTTCCCCGACTGGCAGAACTACACCCCCGGCCCCGGCATCCGCTACCCCCT
GACCTTCGGCTGGTGCTTCAAGCTGGTGCCCGTGGACCCCGCCGAGGTGGAGGAGGCCACCGAGGGCGAGAACAACTCCCTG
CTGCACCCCATCTGCCAGCACGGCATGGACGACGAGGAGCGCGAGGTGCTGATGTGGAAGTTCGACTCCCGCCTGGCCCTGA
AGCACCGCGCCCCGCGAGCTGCACCCCGAGTTCTACAAGGACTGCTAA

3.89 A

36. 2003_CON_A2 nef.PEP

MGGKWSKSSIVGWPAIRERMRKRTPPAAEGVGAVSQDLATRGAVTSSNTAATNPDCAWLEAQEEEEVGFPVRPQVPLRPMTF
KGAFDLSHFLKEKGGLDGLIYSQKRQDILDLWVYHTQGYFPDWQNYTPGPGTRYPLTFGWCFKLVPVDPSEVEEATEGENNS
LLHPICQHGIEDPEREVLRWKFDSRLALRHRARELHPEFYKDC$

B

2003_CON_A2 nef.OPT

ATGGGCGGCAAGTGGTCCAAGTCCTCCATCGTGGGCTGGCCCGCCATCCGCGAGCGCATGCGCAAGCGCACCCCCCCCGCCG
CCGAGGGCGTGGGCGCCGTGTCCCAGGACCTGGCCACCCGCGGCGCCGTGACCTCCTCCAACACCGCCGCCACCAACCCCGA
CTGCGCCTGGCTGGAGGCCCAGGAGGAGGAGGAGGTGGGCTTCCCCGTGCGCCCCCAGGTGCCCCTGCGCCCCATGACCTTC
AAGGGCGCCTTCGACCTGTCCCACTTCCTGAAGGAGAAGGGCGGCCTGGACGGCCTGATCTACTCCCAGAAGCGCCAGGACA
TCCTGGACCTGTGGGTGTACCACACCCAGGGCTACTTCCCCGACTGGCAGAACTACACCCCCGGCCCCGGCACCCGCTACCC
CCTGACCTTCGGCTGGTGCTTCAAGCTGGTGCCCGTGGACCCCTCCGAGGTGGAGGAGGCCACCGAGGGCGAGAACAACTCC
CTGCTGCACCCCATCTGCCAGCACGGCATCGAGGACCCCGAGCGCGAGGTGCTGCGCTGGAAGTTCGACTCCCGCCTGGCCC
TGCGCCACCGCGCCCGCGAGCTGCACCCCGAGTTCTACAAGGACTGCTAA

Fig. 90 A

37. 2003_CON_B nef.PEP

MGGKWSKRSVVGWPTVRERMRRAEPAADGVGAVSRDLEKHGAITSSNTAANNADCAWLEAQEEEEVGFPVRPQVPLRPMTYK
GALDLSHFLKEKGGLEGLIYSQKRQDILDLWVYHTQGYFPDWQNYTPGPGIRYPLTFGWCFKLVPVEPEKVEEANEGENNSL
LHPMSLHGMDDPEREVLVWKFDSRLAFHHMARELHPEYYKDC$

B

2003_CON-B nef.OPT

ATGGGCGGCAAGTGGTCCAAGCGCTCCGTGGTGGGCTGGCCCACCGTGCGCGAGCGCATGCGCCGCGCCGAGCCCGCCGCCG
ACGGCGTGGGCGCCGTGTCCCGCGACCTGGAGAAGCACGGCGCCATCACCTCCTCCAACACCGCCGCCAACAACGCCGACTG
CGCCTGGCTGGAGGCCCAGGAGGAGGAGGAGGTGGGCTTCCCCGTGCGCCCCCAGGTGCCCCTGCGCCCCATGACCTACAAG
GGCGCCCTGGACCTGTCCCACTTCCTGAAGGAGAAGGGCGGCCTGGAGGGCCTGATCTACTCCCAGAAGCGCCAGGACATCC
TGGACCTGTGGGTGTACCACACCCAGGGCTACTTCCCCGACTGGCAGAACTACACCCCCGGCCCCGGCATCCGCTACCCCCT
GACCTTCGGCTGGTGCTTCAAGCTGGTGCCCGTGGAGCCCGAGAAGGTGGAGGAGGCCAACGAGGGCGAGAACAACTCCCTG
CTGCACCCCATGTCCCTGCACGGCATGGACGACCCCGAGCGCGAGGTGCTGGTGTGGAAGTTCGACTCCCGCCTGGCCTTCC
ACCACATGGCCCGCGAGCTGCACCCCGAGTACTACAAGGACTGCTAA

C

38. 2003_B.anc nef.PEP

MGGKWSKSSMGGWPAVRERMKRAEPAADGVGAVSRDLEKHGAITSSNTAATNADCAWLEAQEEEEVGFPVRPQVPLRPMTYK
AALDLSHFLKEKGGLEGLIYSQKRQDILDLWVYHTQGYFPDWQNYTPGPGIRYPLTFGWCFKLVPVEPEKVEEATEGENNSL
LHPMCQHGMDDPEKEVLVWKFDSRLAFHHMARELHPEYYKDC$

D

2003_B.anc nef.OPT

ATGGGCGGCAAGTGGTCCAAGTCCTCCATGGGCGGCTGGCCCGCCGTGCGCGAGCGCATGAAGCGCGCCGAGCCCGCCGCCG
ACGGCGTGGGCGCCGTGTCCCGCGACCTGGAGAAGCACGGCGCCATCACCTCCTCCAACACCGCCGCCACCAACGCCGACTG
CGCCTGGCTGGAGGCCCAGGAGGAGGAGGAGGTGGGCTTCCCCGTGCGCCCCCAGGTGCCCCTGCGCCCCATGACCTACAAG
GCCGCCCTGGACCTGTCCCACTTCCTGAAGGAGAAGGGCGGCCTGGAGGGCCTGATCTACTCCCAGAAGCGCCAGGACATCC
TGGACCTGTGGGTGTACCACACCCAGGGCTACTTCCCCGACTGGCAGAACTACACCCCCGGCCCCGGCATCCGCTACCCCCT
GACCTTCGGCTGGTGCTTCAAGCTGGTGCCCGTGGAGCCCGAGAAGGTGGAGGAGGCCACCGAGGGCGAGAACAACTCCCTG

CTGCACCCCATGTGCCAGCACGGCATGGACGACCCCGAGAAGGAGGTGCTGGTGTGGAAGTTCGACTCCCGCCTGGCCTTCC
ACCACATGGCCCGCGAGCTGCACCCCGAGTACTACAAGGACTGCTAA

Fig. 91A

39. 2003_CON_02_AG nef.PEP

MGGKWSKSSIVGWPKVRERIRQTPPAATGVGAASQDLDRHGAITSSNTAATNADCAWLEAQEEEEVGFPVRPQVPLRPMTYK
AAVDLSHFLKEKGGLEGLIYSKKRQEILDLWVYHTQGFFPDWQNYTPGPGTRFPLTFGWCFKLVPMDPAEVEEANEGENNSL
LHPICQHGMEDEDREVLVWRFDSSLAFKHRARELHPEFYKDC$

2003_CON_02_AG nef.OPT

Fig. 91B

ATGGGCGGCAAGTGGTCCAAGTCCTCCATCGTGGGCTGGCCCAAGGTGCGCGAGCGCATCCGCCAGACCCCCCCCGCCGCCA
CCGGCGTGGGCGCCGCCTCCCAGGACCTGGACCGCCACGGCGCCATCACCTCCTCCAACACCGCCGCCACCAACGCCGACTG
CGCCTGGCTGGAGGCCCAGGAGGAGGAGGAGGTGGGCTTCCCCGTGCGCCCCCAGGTGCCCCTGCGCCCCATGACCTACAAG
GCCGCCGTGGACCTGTCCCACTTCCTGAAGGAGAAGGGCGGCCTGGAGGGCCTGATCTACTCCAAGAAGCGCCAGGAGATCC
TGGACCTGTGGGTGTACCACACCCAGGGCTTCTTCCCCGACTGGCAGAACTACACCCCCGGCCCCGGCACCCGCTTCCCCCT
GACCTTCGGCTGGTGCTTCAAGCTGGTGCCCATGGACCCCGCCGAGGTGGAGGAGGCCAACGAGGGCGAGAACAACTCCCTG
CTGCACCCCATCTGCCAGCACGGCATGGAGGACGAGGACCGCGAGGTGCTGGTGTGGCGCTTCGACTCCTCCCTGGCCTTCA
AGCACCGCGCCCGCGAGCTGCACCCCGAGTTCTACAAGGACTGCTAA

Fig. 92A

40. 2003_CON_C nef.PEP

MGGKWSKSSIVGWPAVRERIRRTEPAAEGVGAASQDLDKHGALTSSNTATNNADCAWLEAQEEEEEVGFPVRPQVPLRPMTY
KAAFDLSFFLKEKGGLEGLIYSKKRQEILDLWVYHTQGYFPDWQNYTPGPGVRYPLTFGWCFKLVPVDPREVEEANEGENNC
LLHPMSQHGMEDEDREVLKWKFDSHLARRHMARELHPEYYKDC$

2003_CON_C nef.OPT

Fig. 92B

ATGGGCGGCAAGTGGTCCAAGTCCTCCATCGTGGGCTGGCCCGCCGTGCGCGAGCGCATCCGCCGCACCGAGCCCGCCGCCG
AGGGCGTGGGCGCCGCCTCCCAGGACCTGGACAAGCACGGCGCCCTGACCTCCTCCAACACCGCCACCAACAACGCCGACTG
CGCCTGGCTGGAGGCCCAGGAGGAGGAGGAGGAGGTGGGCTTCCCCGTGCGCCCCCAGGTGCCCCTGCGCCCCATGACCTAC
AAGGCCGCCTTCGACCTGTCCTTCTTCCTGAAGGAGAAGGGCGGCCTGGAGGGCCTGATCTACTCCAAGAAGCGCCAGGAGA
TCCTGGACCTGTGGGTGTACCACACCCAGGGCTACTTCCCCGACTGGCAGAACTACACCCCCGGCCCCGGCGTGCGCTACCC
CCTGACCTTCGGCTGGTGCTTCAAGCTGGTGCCCGTGGACCCCCGCGAGGTGGAGGAGGCCAACGAGGGCGAGAACAACTGC
CTGCTGCACCCCATGTCCCAGCACGGCATGGAGGACGAGGACCGCGAGGTGCTGAAGTGGAAGTTCGACTCCCACCTGGCCC
GCCGCCACATGGCCCGCGAGCTGCACCCCGAGTACTACAAGGACTGCTAA

Fig. 93C

41. 2003_C.anc nef.PEP

MGGKWSKSSIVGWPAVRERMRRTEPAAEGVGAASQDLDKHGALTSSNTAANNADCAWLEAQEEEEEVGFPVRPQVPLRPMTY
KAAFDLSFFLKEKGGLDGLIYSKKRQEILDLWVYHTQGYFPDWQNYTPGPGVRYPLTFGWCFKLVPVDPREVEEANEGENNC
LLHPMSQHGMEDEDREVLKWKFDSHLARRHMARELHPEYYKDC$

2003_C.anc nef.OPT

Fig. 93D

ATGGGCGGCAAGTGGTCCAAGTCCTCCATCGTGGGCTGGCCCGCCGTGCGCGAGCGCATGCGCCGCACCGAGCCCGCCGCCG
AGGGCGTGGGCGCCGCCTCCCAGGACCTGGACAAGCACGGCGCCCTGACCTCCTCCAACACCGCCGCCAACAACGCCGACTG
CGCCTGGCTGGAGGCCCAGGAGGAGGAGGAGGAGGTGGGCTTCCCCGTGCGCCCCCAGGTGCCCCTGCGCCCCATGACCTAC
AAGGCCGCCTTCGACCTGTCCTTCTTCCTGAAGGAGAAGGGCGGCCTGGACGGCCTGATCTACTCCAAGAAGCGCCAGGAGA
TCCTGGACCTGTGGGTGTACCACACCCAGGGCTACTTCCCCGACTGGCAGAACTACACCCCCGGCCCCGGCGTGCGCTACCC
CCTGACCTTCGGCTGGTGCTTCAAGCTGGTGCCCGTGGACCCCCGCGAGGTGGAGGAGGCCAACGAGGGCGAGAACAACTGC
CTGCTGCACCCCATGTCCCAGCACGGCATGGAGGACGAGGACCGCGAGGTGCTGAAGTGGAAGTTCGACTCCCACCTGGCCC
GCCGCCACATGGCCCGCGAGCTGCACCCCGAGTACTACAAGGACTGCTAA

Fig. 93A

42. 2003_CON_D nef.PEP

MGGKWSKSSIVGWPAIRERIRRTEPAADGVGAVSRDLEKHGAITSSNTAATNADCAWLEAQEEDEEVGFPVRPQVPLRPMTY
KAALDLSHFLKEKGGLEGLVWSQKRQEILDLWVYNTQGFFPDWQNYTPGPGIRYPLTFGWCFELVPVDPEEVEEATEGENNC
LLHPMCQHGMEDPEREVLMWRFNSRLAFEHKARVLHPEFYKDC$

2003_CON_D nef.OPT

Fig. 93B

ATGGGCGGCAAGTGGTCCAAGTCCTCCATCGTGGGCTGGCCCGCCATCCGCGAGCGCATCCGCCGCACCGAGCCCGCCGCCG
ACGGCGTGGGCGCCGTGTCCCGCGACCTGGAGAAGCACGGCGCCATCACCTCCTCCAACACCGCCGCCACCAACGCCGACTG
CGCCTGGCTGGAGGCCCAGGAGGAGGACGAGGAGGTGGGCTTCCCCGTGCGCCCCCAGGTGCCCCTGCGCCCCATGACCTAC
AAGGCCGCCCTGGACCTGTCCCACTTCCTGAAGGAGAAGGGCGGCCTGGAGGGCCTGGTGTGGTCCCAGAAGCGCCAGGAGA
TCCTGGACCTGTGGGTGTACAACACCCAGGGCTTCTTCCCCGACTGGCAGAACTACACCCCCGGCCCCGGCATCCGCTACCC

CCTGACCTTCGGCTGGTGCTTCGAGCTGGTGCCCGTGGACCCCGAGGAGGTGGAGGAGGCCACCGAGGGCGAGAACAACTGC
CTGCTGCACCCCATGTGCCAGCACGGCATGGAGGACCCCGAGCGCGAGGTGCTGATGTGGCGCTTCAACTCCCGCCTGGCCT
TCGAGCACAAGGCCCGCGTGCTGCACCCCGAGTTCTACAAGGACTGCTAA

1.94A

43. 2003_CON_F1 nef.PEP

MGGKWSKSSIVGWPAVRERMRPTPPAAEGVGAVSQDLERRGAITSSNTGATNPDLAWLEAQEEEEVGFPVRPQVPLRPMTYK
GAVDLSHFLKEKGGLEGLIYSKKRQEILDLWVYHTQGYFPDWQNYTPGPGIRYPLTFGWCFKLVPVDPEEVEKANEGENNCL
LHPMSQHGMEDEDREVLIWKFDSRLALRHIARERHPEFYQD$

2003_CON_F1 nef.OPT

B

ATGGGCGGCAAGTGGTCCAAGTCCTCCATCGTGGGCTGGCCCGCCGTGCGCGAGCGCATGCGCCCCACCCCCCCCGCCGCCG
AGGGCGTGGGCGCCGTGTCCCAGGACCTGGAGCGCCGCGGCGCCATCACCTCCTCCAACACCGGCGCCACCAACCCCGACCT
GGCCTGGCTGGAGGCCCAGGAGGAGGAGGAGGTGGGCTTCCCCGTGCGCCCCCAGGTGCCCCTGCGCCCCATGACCTACAAG
GGCGCCGTGGACCTGTCCCACTTCCTGAAGGAGAAGGGCGGCCTGGAGGGCCTGATCTACTCCAAGAAGCGCCAGGAGATCC
TGGACCTGTGGGTGTACCACACCCAGGGCTACTTCCCCGACTGGCAGAACTACACCCCCGGCCCCGGCATCCGCTACCCCCT
GACCTTCGGCTGGTGCTTCAAGCTGGTGCCCGTGGACCCCGAGGAGGTGGAGAAGGCCAACGAGGGCGAGAACAACTGCCTG
CTGCACCCCATGTCCCAGCACGGCATGGAGGACGAGGACCGCGAGGTGCTGATCTGGAAGTTCGACTCCCGCCTGGCCCTGC
GCCACATCGCCCGCGAGCGCCACCCCGAGTTCTACCAGGACTAA

2.95A

44. 2003_CON_F2 nef.PEP

MGGKWSKSSIVGWPTIRERIRRTPVAAEGVGAVSQDLDKHGAITSSNTRATNADLAWLEAQEDEEVGFPVRPQVPLRPMTYK
AAFDLSHFLKEKGGLEGLIYSKKRQEILDLWVYHTQGYFPDWQNYTPGPGTRYPLTFGWCFKLVPVDPEEVEKANEGENNCL
LHPMSLHGMEDEDREVLKWKFDSRLALRHIARERHPEYYKD$

2003_CON_F2 nef.OPT

B

ATGGGCGGCAAGTGGTCCAAGTCCTCCATCGTGGGCTGGCCCACCATCCGCGAGCGCATCCGCCGCACCCCCGTGGCCGCCG
AGGGCGTGGGCGCCGTGTCCCAGGACCTGGACAAGCACGGCGCCATCACCTCCTCCAACACCCGCGCCACCAACGCCGACCT
GGCCTGGCTGGAGGCCCAGGAGGACGAGGAGGTGGGCTTCCCCGTGCGCCCCCAGGTGCCCCTGCGCCCCATGACCTACAAG
GCCGCCTTCGACCTGTCCCACTTCCTGAAGGAGAAGGGCGGCCTGGAGGGCCTGATCTACTCCAAGAAGCGCCAGGAGATCC
TGGACCTGTGGGTGTACCACACCCAGGGCTACTTCCCCGACTGGCAGAACTACACCCCCGGCCCCGGCACCCGCTACCCCCT
GACCTTCGGCTGGTGCTTCAAGCTGGTGCCCGTGGACCCCGAGGAGGTGGAGAAGGCCAACGAGGGCGAGAACAACTGCCTG
CTGCACCCCATGTCCCTGCACGGCATGGAGGACGAGGACCGCGAGGTGCTGAAGTGGAAGTTCGACTCCCGCCTGGCCCTGC
GCCACATCGCCCGCGAGCGCCACCCCGAGTACTACAAGGACTAA

9.96A

45. 2003_CON_G nef.PEP

MGGKWSKSSIVGWPEVRERIRQTPPAAEGVGAVSQDLARHGAITSSNTAANNPDCAWLEAQEEDSEVGFPVRPQVPLRPMTY
KGAFDLSFFLKEKGGLDGLIYSKKRQDILDLWVYNTQGFFPDWQNYTPGPGTRFPLTFGWCFKLVPMDPAEVEEANKGENNS
LLHPICQHGMEDEDREVLVWRFDSSLARRHIARELHPEYYKDC$

2003_CON_G nef.OPT

B

ATGGGCGGCAAGTGGTCCAAGTCCTCCATCGTGGGCTGGCCCGAGGTGCGCGAGCGCATCCGCCAGACCCCCCCCGCCGCCG
AGGGCGTGGGCGCCGTGTCCCAGGACCTGGCCCGCCACGGCGCCATCACCTCCTCCAACACCGCCGCCAACAACCCCGACTG
CGCCTGGCTGGAGGCCCAGGAGGAGGACTCCGAGGTGGGCTTCCCCGTGCGCCCCCAGGTGCCCCTGCGCCCCATGACCTAC
AAGGGCGCCTTCGACCTGTCCTTCTTCCTGAAGGAGAAGGGCGGCCTGGACGGCCTGATCTACTCCAAGAAGCGCCAGGACA
TCCTGGACCTGTGGGTGTACAACACCCAGGGCTTCTTCCCCGACTGGCAGAACTACACCCCCGGCCCCGGCACCCGCTTCCC
CCTGACCTTCGGCTGGTGCTTCAAGCTGGTGCCCATGGACCCCGCCGAGGTGGAGGAGGCCAACAAGGGCGAGAACAACTCC
CTGCTGCACCCCATCTGCCAGCACGGCATGGAGGACGAGGACCGCGAGGTGCTGGTGTGGCGCTTCGACTCCTCCCTGGCCC
GCCGCCACATCGCCCGCGAGCTGCACCCCGAGTACTACAAGGACTGCTAA

Fig. 97A

46. 2003_CON_H nef.PEP

MGGKWSKSSIGGWPAIRERIRRAEPAAEGVGAVSRDLDRRGAVTINNTASTNPDSAWLEAQEEEEEVGFPVRPQVPLRPMTY
KGAFDLSHFLKEKGGLEGLIYSKKRQEILDLWVYNTQGYFPDWQNYTPGPGERYPLTFGWCFKLVPVDPQEVEKANEGENNS
LLHPICQHGMEDEEREVLMWKFDSRLAFRHIARELHPEFYKDC$

2003_CON_H nef.OPT

B

ATGGGCGGCAAGTGGTCCAAGTCCTCCATCGGCGGCTGGCCCGCCATCCGCGAGCGCATCCGCCGCGCCGAGCCCGCCGCCG
AGGGCGTGGGCGCCGTGTCCCGCGACCTGGACCGCCGCGGCGCCGTGACCATCAACAACACCGCCTCCACCAACCCCGACTC
CGCCTGGCTGGAGGCCCAGGAGGAGGAGGAGGTGGGCTTCCCCGTGCGCCCCCAGGTGCCCCTGCGCCCCATGACCTAC
AAGGGCGCCTTCGACCTGTCCCACTTCCTGAAGGAGAAGGGCGGCCTGGAGGGCCTGATCTACTCCAAGAAGCGCCAGGAGA

TCCTGGACCTGTGGGTGTACAACACCCAGGGCTACTTCCCCGACTGGCAGAACTACACCCCCGGCCCCGGCGAGCGCTACCC
CCTGACCTTCGGCTGGTGCTTCAAGCTGGTGCCCGTGGACCCCCAGGAGGTGGAGAAGGCCAACGAGGGCGAGAACAACTCC
CTGCTGCACCCCATCTGCCAGCACGGCATGGAGGACGAGGAGCGCGAGGTGCTGATGTGGAAGTTCGACTCCCGCCTGGCCT
TCCGCCACATCGCCCGCGAGCTGCACCCCGAGTTCTACAAGGACTGCTAA

Fig. 98 A

47. 2003_CON_01_AE nef.PEP

MGGKWSKSSIVGWPQVRERIKQTPPATEGVGAVSQDLDKHGAVTSSNMNNADCVWLRAQEEEEVGFPVRPQVPLRPMTYKGA
FDLSFFLKEKGGLDGLIYSKKRQEILDLWVYNTQGFFPDWQNYTPGPGIRYPLCFGWCFKLVPVDPREVEEDNKGENNCLLH
PMSQHGIEDEEREVLMWKFDSALARKHIARELHPEYYKDC$

2003_CON_01_AE nef.OPT

B

ATGGGCGGCAAGTGGTCCAAGTCCTCCATCGTGGGCTGGCCCCAGGTGCGCGAGCGCATCAAGCAGACCCCCCCCGCCACCG
AGGGCGTGGGCGCCGTGTCCCAGGACCTGGACAAGCACGGCGCCGTGACCTCCTCCAACATGAACAACGCCGACTGCGTGTG
GCTGCCGCGCCCAGGAGGAGGAGGAGGTGGGCTTCCCCGTGCGCCCCCAGGTGCCCCTGCGCCCCATGACCTACAAGGGCGCC
TTCGACCTGTCCTTCTTCCTGAAGGAGAAGGGCGGCCTGGACGGCCTGATCTACTCCAAGAAGCGCCAGGAGATCCTGGACC
TGTGGGTGTACAACACCCAGGGCTTCTTCCCCGACTGGCAGAACTACACCCCCGGCCCCGGCATCCGCTACCCCCTGTGCTT
CGGCTGGTGCTTCAAGCTGGTGCCCGTGGACCCCCGCGAGGTGGAGGAGGACAACAAGGGCGAGAACAACTGCCTGCTGCAC
CCCATGTCCCAGCACGGCATCGAGGACGAGGAGCGCGAGGTGCTGATGTGGAAGTTCGACTCCGCCCTGGCCCGCAAGCACA
TCGCCCGCGAGCTGCACCCCGAGTACTACAAGGACTGCTAA

Fig. 99 A

48. 2003_CON_03_AE nef.PEP

MGGKWSKSSIVGWPQVRERIRRAPAPAARGVGPVSQDLDKYGAVTSSNTAANNADCAWLEAQKEEEVGFPVRPQVPLRPMTY
KGAFDLSHFLKEKGGLDGLIYSKKRQEILDLWVYHTQGYFPDWQNYTPGPGIRFPLTFGWCYKLVPVDPDEVEEATEGENNS
LLHPICQHGMDDEEKEVLMWKFDSRLALTHRARELHPEFYKDC$

2003_CON_03_AE nef.OPT

B

ATGGGCGGCAAGTGGTCCAAGTCCTCCATCGTGGGCTGGCCCCAGGTGCGCGAGCGCATCCGCCGCGCCCCCGCCCCCGCCG
CCCGCGGCGTGGGCCCCGTGTCCCAGGACCTGGACAAGTACGGCGCCGTGACCTCCTCCAACACCGCCGCCAACAACGCCGA
CTGCGCCTGGCTGGAGGCCCAGAAGGAGGAGGAGGTGGGCTTCCCCGTGCGCCCCCAGGTGCCCCTGCGCCCCATGACCTAC
AAGGGCGCCTTCGACCTGTCCCACTTCCTGAAGGAGAAGGGCGGCCTGGACGGCCTGATCTACTCCAAGAAGCGCCAGGAGA
TCCTGGACCTGTGGGTGTACCACACCCAGGGCTACTTCCCCGACTGGCAGAACTACACCCCCGGCCCCGGCATCCGCTTCCC
CCTGACCTTCGGCTGGTGCTACAAGCTGGTGCCCGTGGACCCCGACGAGGTGGAGGAGGCCACCGAGGGCGAGAACAACTCC
CTGCTGCACCCCATCTGCCAGCACGGCATGGACGACGAGGAGAAGGAGGTGCTGATGTGGAAGTTCGACTCCCGCCTGGCCC
TGACCCACCGCGCCCGCGAGCTGCACCCCGAGTTCTACAAGGACTGCTAA

Fig. 100 A

49. 2003_CON_04_CFX nef.PEP

MGGKWSKSSIVGWPAIRERMRQRGPAQAEPAAAGVGAVSQDLDKHGAITSSNTAATNPDKAWLEAQEEEEEVGFPVRPQVPL
RPMTFKAALDLSHFLKEKGGLDGLIYSKKRQEILDLWVYNTQGYFPDWQNYTPGPGERFPLCFGWCFKLVPVDPQEVEEATE
GENNCLLHPISQHGMEDEEREVLKWKFDSRLAYKHIARELHPEFYKDC$

2003_CON_04_CFX nef.OPT

B

ATGGGCGGCAAGTGGTCCAAGTCCTCCATCGTGGGCTGGCCCGCCATCCGCGAGCGCATGCGCCAGCGCGGCCCCGCCCAGG
CCGAGCCCGCCGCCGCCGGCGTGGGCGCCGTGTCCCAGGACCTGGACAAGCACGGCGCCATCACCTCCTCCAACACCGCCGC
CACCAACCCCGACAAGGCCTGGCTGGAGGCCCAGGAGGAGGAGGAGGAGGTGGGCTTCCCCGTGCGCCCCCAGGTGCCCCTG
CGCCCCATGACCTTCAAGGCCGCCCTGGACCTGTCCCACTTCCTGAAGGAGAAGGGCGGCCTGGACGGCCTGATCTACTCCA
AGAAGCGCCAGGAGATCCTGGACCTGTGGGTGTACAACACCCAGGGCTACTTCCCCGACTGGCAGAACTACACCCCCGGCCC
CGGCGAGCGCTTCCCCCTGTGCTTCGGCTGGTGCTTCAAGCTGGTGCCCGTGGACCCCCAGGAGGTGGAGGAGGCCACCGAG
GGCGAGAACAACTGCCTGCTGCACCCCATCTCCCAGCACGGCATGGAGGACGAGGAGCGCGAGGTGCTGAAGTGGAAGTTCG
ACTCCCGCCTGGCCTACAAGCACATCGCCCGCGAGCTGCACCCCGAGTTCTACAAGGACTGCTAA

Fig. 101 A

50. 2003_CON_06_CFX nef.PEP

MGGKWSKSSIVGWPQVRERMRNPPTEGAAEGVGAVSQDLDKHGAITSSNTATTNAACAWLEAQTEDEVGFPVRPQVPLRPMT
YKGAFDLSFFLKEKGGLDGLIYSKKRQEILDLWVYHTQGFPPDWQNYTPGPGIRYPLTFGWCYKLVPVDPKEVEEDTKGENN
CLLHPMCQHGVEDEEREVLMWKFDSSLARRHIAREMHPEFYKDC$

2003_CON_06_CFX nef.OPT

B

ATGGGCGGCAAGTGGTCCAAGTCCTCCATCGTGGGCTGGCCCCAGGTGCGCGAGCGCATGCGCAACCCCCCCCACCGAGGGCG
CCGCCGAGGGCGTGGGCGCCGTGTCCCAGGACCTGGACAAGCACGGCGCCATCACCTCCTCCAACACCGCCACCACCAACGC
CGCCTGCGCCTGGCTGGAGGCCCAGACCGAGGACGAGGTGGGCTTCCCCGTGCGCCCCCAGGTGCCCCTGCGCCCCATGACC

TACAAGGGCGCCTTCGACCTGTCCTTCTTCCTGAAGGAGAAGGGCGGCCTGGACGGCCTGATCTACTCCAAGAAGCGCCAGG
AGATCCTGGACCTGTGGGTGTACCACACCCAGGGCTTCTTCCCCGACTGGCAGAACTACACCCCCGGCCCCGGCATCCGCTA
CCCCCTGACCTTCGGCTGGTGCTACAAGCTGGTGCCCGTGGACCCCAAGGAGGTGGAGGAGGACACCAAGGGCGAGAACAAC
TGCCTGCTGCACCCCATGTGCCAGCACGGCGTGGAGGACGAGGAGCGCGAGGTGCTGATGTGGAAGTTCGACTCCTCCCTGG
CCCGCCGCCACATCGCCCGCGAGATGCACCCCGAGTTCTACAAGGACTGCTAA

q.102 A

51. 2003_CON_08_BC nef.PEP

MGGKWSKSSIVGWPAIRERIRRTEPAADGVGAVSRDLEKHGAITSSNTADTNADCAWLETQEEEEVGFPVRPQVPLRPMTFK
GALDLSFFLKEKGGLEGLIYSKKRQEILDLWVYHTQGYFPDWHNYTPGPGVRFPLTFGWCFKLVPVDPREVEEANEGEDNCL
LHPVCQHGMEDEHREVLKWKFDSQLAHRHRARELHPEFYKDC$

2003_CON_08_BC nef.OPT

B

ATGGGCGGCAAGTGGTCCAAGTCCTCCATCGTGGGCTGGCCCGCCATCCGCGAGCGCATCCGCCGCACCGAGCCCGCCGCCG
ACGGCGTGGGCGCCGTGTCCCGCGACCTGGAGAAGCACGGCGCCATCACCTCCTCCAACACCGCCGACACCAACGCCGACTG
CGCCTGGCTGGAGACCCAGGAGGAGGAGGAGGTGGGCTTCCCCGTGCGCCCCCAGGTGCCCCTGCGCCCCATGACCTTCAAG
GGCGCCCTGGACCTGTCCTTCTTCCTGAAGGAGAAGGGCGGCCTGGAGGGCCTGATCTACTCCAAGAAGCGCCAGGAGATCC
TGGACCTGTGGGTGTACCACACCCAGGGCTACTTCCCCGACTGGCACAACTACACCCCCGGCCCCGGCGTGCGCTTCCCCCT
GACCTTCGGCTGGTGCTTCAAGCTGGTGCCCGTGGACCCCCGCGAGGTGGAGGAGGCCAACGAGGGCGAGGACAACTGCCTG
CTGCACCCCGTGTGCCAGCACGGCATGGAGGACGAGCACCGCGAGGTGCTGAAGTGGAAGTTCGACTCCCAGCTGGCCCACC
GCCACCGCGCCCGCGAGCTGCACCCCGAGTTCTACAAGGACTGCTAA

q.103 A

52. 2003_CON_10_CD nef.PEP

MGGKWSKSSIVGWPAVRERIRRTDPAAEGVGAASRDLEKYGAITSSNTAQTNPDCAWLEAQEEEEEVGFPVRPQVPLRPMTY
KGAFDLSFFLKEKGGLEGLIYSKRRQDILDLWVYNTQGFFPDWQNYTPGPGIRYPLTFGWCYKLVPVDPREVEEANEGENNS
LLHPMSLHGMEDPHGEVLMWKFDSNLAHKHMARELHPEYYKDC$

2003_CON_10_CD nef.OPT

B

ATGGGCGGCAAGTGGTCCAAGTCCTCCATCGTGGGCTGGCCCGCCGTGCGCGAGCGCATCCGCCGCACCGACCCCGCCGCCG
AGGGCGTGGGCGCCGCCTCCCGCGACCTGGAGAAGTACGGCGCCATCACCTCCTCCAACACCGCCCAGACCAACCCCGACTG
CGCCTGGCTGGAGGCCCAGGAGGAGGAGGAGGAGGTGGGCTTCCCCGTGCGCCCCCAGGTGCCCCTGCGCCCCATGACCTAC
AAGGGCGCCTTCGACCTGTCCTTCTTCCTGAAGGAGAAGGGCGGCCTGGAGGGCCTGATCTACTCCAAGCGCCGCCAGGACA
TCCTGGACCTGTGGGTGTACAACACCCAGGGCTTCTTCCCCGACTGGCAGAACTACACCCCCGGCCCCGGCATCCGCTACCC
CCTGACCTTCGGCTGGTGCTACAAGCTGGTGCCCGTGGACCCCCGCGAGGTGGAGGAGGCCAACGAGGGCGAGAACAACTCC
CTGCTGCACCCCATGTCCCTGCACGGCATGGAGGACCCCCACGGCGAGGTGCTGATGTGGAAGTTCGACTCCAACCTGGCCC
ACAAGCACATGGCCCGCGAGCTGCACCCCGAGTACTACAAGGACTGCTAA

q.104 A

53. 2003_CON_11_CFX nef.PEP

MGGKWSKSSIVGWPEIRERLRRTPPTAAAEGVGAVSKDLEKHGAVTSSNTAQTNAACAWLEAQEEEEVGFPVRPQVPLRPMT
YKGAFDLGFFLKEKGGLDGLIYSKKRQEILDLWVYHTQGYFPDWQNYTPGPGIRYPLCFGWCFKLVPVEPREVEEANEGENN
CLLHPMSQHGMDDEEREVLMWKFDSSLARRHIARELHPDFYKDC$

2003_CON_11_CFX nef.OPT

B

ATGGGCGGCAAGTGGTCCAAGTCCTCCATCGTGGGCTGGCCCGAGATCCGCGAGCGCCTGCGCCGCACCCCCCCCCACCGCCG
CCGCCGAGGGCGTGGGCGCCGTGTCCAAGGACCTGGAGAAGCACGGCGCCGTGACCTCCTCCAACACCGCCCAGACCAACGC
CGCCTGCGCCTGGCTGGAGGCCCAGGAGGAGGAGGAGGAGGTGGGCTTCCCCGTGCGCCCCCAGGTGCCCCTGCGCCCCATGACC
TACAAGGGCGCCTTCGACCTGGGCTTCTTCCTGAAGGAGAAGGGCGGCCTGGACGGCCTGATCTACTCCAAGAAGCGCCAGG
AGATCCTGGACCTGTGGGTGTACCACACCCAGGGCTACTTCCCCGACTGGCAGAACTACACCCCCGGCCCCGGCATCCGCTA
CCCCCTGTGCTTCGGCTGGTGCTTCAAGCTGGTGCCCGTGGAGCCCCGCGAGGTGGAGGAGGCCAACGAGGGCGAGAACAAC
TGCCTGCTGCACCCCATGTCCCAGCACGGCATGGACGACGAGGAGCGCGAGGTGCTGATGTGGAAGTTCGACTCCTCCCTGG
CCCGCCGCCACATCGCCCGCGAGCTGCACCCCGACTTCTACAAGGACTGCTAA

q.105 A

54. 2003_CON_12_BF nef.PEP

MGGKWSKSSIVGWPDIRERMRRAPPAAEGVGAVSQDLENRGAITSSNTRANNPDLAWLEAQEEEEVGFPVRPQVPLRPMTYK
GALDLSHFLKEKGGLEGLIYSKKRQEILDLWVYHTQGYFPDWQNYTPGPGIRYPLTFGWCFKLVPVDPEEVEKANEGENNCL
LHPMSQHGMEDEDREVLMWKFDSRLALRHIAREKHPEFYQDC$

2003_CON_12_BF nef.OPT

B

ATGGGCGGCAAGTGGTCCAAGTCCTCCATCGTGGGCTGGCCCGACATCCGCGAGCGCATGCGCCGCGCCCCCCCCCGCCGCCG
AGGGCGTGGGCGCCGTGTCCCAGGACCTGGAGAACCGCGGCGCCATCACCTCCTCCAACACCCGCGCCAACAACCCCGACCT

GGCCTGGCTGGAGGCCCAGGAGGAGGAGGAGGTGGGCTTCCCCGTGCGCCCCCAGGTGCCCCTGCGCCCCATGACCTACAAG
GGCGCCCTGGACCTGTCCCACTTCCTGAAGGAGAAGGGCGGCCTGGAGGGCCTGATCTACTCCAAGAAGCGCCAGGAGATCC
TGGACCTGTGGGTGTACCACACCCAGGGCTACTTCCCCGACTGGCAGAACTACACCCCCGGCCCCGGCATCCGCTACCCCCT
GACCTTCGGCTGGTGCTTCAAGCTGGTGCCCGTGGACCCCGAGGAGGTGGAGAAGGCCAACGAGGGCGAGAACAACTGCCTG
CTGCACCCCATGTCCCAGCACGGCATGGAGGACGAGGACCGCGAGGTGCTGATGTGGAAGTTCGACTCCCGCCTGGCCCTGC
GCCACATCGCCCGCGAGAAGCACCCCGAGTTCTACCAGGACTGCTAA

1,106 A

55. 2003_CON_14_BG nef.PEP

MGGKWSKCSIVGWPEVRERIRRTPPAAVGVGAVSQDLAKHGAITSSNTAANNPDCAWLEAQEEDSEVGFPVRPQVPLRPMTY
KGAFDLSFFLKEKGGLDGLIYSKQRQDILDLWVYNTQGFFPDWQNYTPGPGTRYPLTFGWCFKLEPVDPAEVEEATKGENNS
LLHPICQHGMEDADNEVLIWRFDSSLARRHIARELHPDFYKDC$

2003_CON_14_BG nef.OPT

B

ATGGGCGGCAAGTGGTCCAAGTGCTCCATCGTGGGCTGGCCCGAGGTGCGCGAGCGCATCCGCCGCACCCCCCCCGCCGCCG
TGGGCGTGGGCGCCGTGTCCCAGGACCTGGCCAAGCACGGCGCCATCACCTCCTCCAACACCGCCGCCAACAACCCCGACTG
CGCCTGGCTGGAGGCCCAGGAGGAGGACTCCGAGGTGGGCTTCCCCGTGCGCCCCCAGGTGCCCCTGCGCCCCATGACCTAC
AAGGGCGCCTTCGACCTGTCCTTCTTCCTGAAGGAGAAGGGCGGCCTGGACGGCCTGATCTACTCCAAGCAGCGCCAGGACA
TCCTGGACCTGTGGGTGTACAACACCCAGGGCTTCTTCCCCGACTGGCAGAACTACACCCCCGGCCCCGGCACCCGCTACCC
CCTGACCTTCGGCTGGTGCTTCAAGCTGGAGCCCGTGGACCCCGCCGAGGTGGAGGAGGCCACCAAGGGCGAGAACAACTCC
CTGCTGCACCCCATCTGCCAGCACGGCATGGAGGACGCCGACAACGAGGTGCTGATCTGGCGCTTCGACTCCTCCCTGGCCC
GCCGCCACATCGCCCGCGAGCTGCACCCCGACTTCTACAAGGACTGCTAA

Fig. 107

A

61. 2003_2003_CON_S pol.PEP

FFRENLAFQQGEAREFSSEQTRANSPTSRELRVRGGDNPLSEAGAERQGTVSLSFPQITLWQRPLVTVKIGGQLKEALLDTG
ADDTVLEEINLPGKWKPKMIGGIGGFIKVRQYDQILIEICGKKAIGTVLVGPTPVNIIGRNMLTQIGCTLNFPISPIETVPV
KLKPGMDGPKVKQWPLTEEKIKALTEICTEMEKEGKISKIGPENPYNTPIFAIKKKDSTKWRKLVDFRELNKRTQDFWEVQL
GIPHPAGLKKKKSVTVLDVGDAYFSVPLDEDFRKYTAFTIPSINNETPGIRYQYNVLPQGWKGSPAIFQSSMTKILEPFRTQ
NPEIVIYQYMDDLYVGSDLEIGQHRTKIEELREHLLRWGFTTPDKKHQKEPPFLWMGYELHPDKWTVQPIQLPEKDSWTVND
IQKLVGKLNWASQIYPGIKVKQLCKLLRGAKALTDIVPLTEEAELELAENREILKEPVHGVYYDPSKDLIAEIQKQGQDQWT
YQIYQEPFKNLKTGKYAKMRSAHTNDVKQLTEAVQKIATESIVIWGKTPKFRLPIQKETWETWWTEYWQATWIPEWEFVNTP
PLVKLWYQLEKEPIVGAETFYVDGAANRETKLGKAGYVTDRGRQKVVSLTETTNQKTELQAIHLALQDSGSEVNIVTDSQYA
LGIIQAQPDKSESELVNQIIEQLIKKEKVYLSWVPAHKGIGGNEQVDKLVSTGIRKVLFLDGIDKAQEEHEKYHSNWRAMAS
DFNLPPIVAKEIVASCDKCQLKGEAMHGQVDCSPGIWQLDCTHLEGKIILVAVHVASGYIEAEVIPAETGQETAYFILKLAG
RWPVKVIHTDNGSNFTSAAVKAACWWAGIQQEFGIPYNPQSQGVVESMNKELKKIIGQVRDQAEHLKTAVQMAVFIHNFKRK
GGIGGYSAGERIIDIIATDIQTKELQKQITKIQNFRVYYRDSRDPIWKGPAKLLWKGEGAVVIQDNSEIKVVPRRKAKIIRD
YGKQMAGDDCVAGRQDED$

2003_CON_S pol.OPT

B

TTCTTCCGCGAGAACCTGGCCTTCCAGCAGGGCGAGGCCCGCGAGTTCTCCTCCGAGCAGACCCGCGCCAACTCCCCCACCT
CCCGCGAGCTGCGCGTGCGCGGCGGCGACAACCCCCTGTCCGAGGCCGGCGCCGAGCGCCAGGGCACCGTGTCCCTGTCCTT
CCCCCAGATCACCCTGTGGCAGCGCCCCCTGGTGACCGTGAAGATCGGCGGCCAGCTGAAGGAGGCCCTGCTGGACACCGGC
GCCGACGACACCGTGCTGGAGGAGATCAACCTGCCCGGCAAGTGGAAGCCCAAGATGATCGGCGGCATCGGCGGCTTCATCA
AGGTGCGCCAGTACGACCAGATCCTGATCGAGATCTGCGGCAAGAAGGCCATCGGCACCGTGCTGGTGGGCCCCACCCCCGT
GAACATCATCGGCCGCAACATGCTGACCCAGATCGGCTGCACCCTGAACTTCCCCATCTCCCCCATCGAGACCGTGCCCGTG
AAGCTGAAGCCCGGCATGGACGGCCCCAAGGTGAAGCAGTGGCCCCTGACCGAGGAGAAGATCAAGGCCCTGACCGAGATCT
GCACCGAGATGGAGAAGGAGGGCAAGATCTCCAAGATCGGCCCCGAGAACCCCTACAACACCCCCATCTTCGCCATCAAGAA
GAAGGACTCCACCAAGTGGCGCAAGCTGGTGGACTTCCGCGAGCTGAACAAGCGCACCCAGGACTTCTGGGAGGTGCAGCTG
GGCATCCCCCACCCCGCCGGCCTGAAGAAGAAGAAGTCCGTGACCGTGCTGGACGTGGGCGACGCCTACTTCTCCGTGCCCC
TGGACGAGGACTTCCGCAAGTACACCGCCTTCACCATCCCCTCCATCAACAACGAGACCCCCGGCATCCGCTACCAGTACAA
CGTGCTGCCCCAGGGCTGGAAGGGCTCCCCCCGCCATCTTCCAGTCCTCCATGACCAAGATCCTGGAGCCCTTCCGCACCCAG
AACCCCGAGATCGTGATCTACCAGTACATGGACGACCTGTACGTGGGCTCCGACCTGGAGATCGGCCAGCACCGCACCAAGA
TCGAGGAGCTGCGCGAGCACCTGCTGCGCTGGGGCTTCACCACCCCCGACAAGAAGCACCAGAAGGAGCCCCCCTTCCTGTG
GATGGGCTACGAGCTGCACCCCGACAAGTGGACCGTGCAGCCCATCCAGCTGCCCGAGAAGGACTCCTGGACCGTGAACGAC
ATCCAGAAGCTGGTGGGCAAGCTGAACTGGGCCTCCCAGATCTACCCCGGCATCAAGGTGAAGCAGCTGTGCAAGCTGCTGC
GCGGCGCCAAGGCCCTGACCGACATCGTGCCCCTGACCGAGGAGGCCGAGCTGGAGCTGGCCGAGAACCGCGAGATCCTGAA
GGAGCCCGTGCACGGCGTGTACTACGACCCCTCCAAGGACCTGATCGCCGAGATCCAGAAGCAGGGCCAGGACCAGTGGACC
TACCAGATCTACCAGGAGCCCTTCAAGAACCTGAAGACCGGCAAGTACGCCAAGATGCGCTCCGCCCACACCAACGACGTGA
AGCAGCTGACCGAGGCCGTGCAGAAGATCGCCACCGAGTCCATCGTGATCTGGGGCAAGACCCCCAAGTTCCGCCTGCCCAT
CCAGAAGGAGACCTGGGAGACCTGGTGGACCGAGTACTGGCAGGCCACCTGGATCCCCGAGTGGGAGTTCGTGAACACCCCC
CCCCTGGTGAAGCTGTGGTACCAGCTGGAGAAGGAGCCCATCGTGGGCGCCGAGACCTTCTACGTGGACGGCGCCGCCAACC
GCGAGACCAAGCTGGGCAAGGCCGGCTACGTGACCGACCGCGGCCGCCAGAAGGTGGTGTCCCTGACCGAGACCACCAACCA
GAAGACCGAGCTGCAGGCCATCCACCTGGCCCTGCAGGACTCCGGCTCCGAGGTGAACATCGTGACCGACTCCCAGTACGCC
CTGGGCATCATCCAGGCCCAGCCCGACAAGTCCGAGTCCGAGCTGGTGAACCAGATCATCGAGCAGCTGATCAAGAAGGAGA
AGGTGTACCTGTCCTGGGTGCCCGCCCACAAGGGCATCGGCGGCAACGAGCAGGTGGACAAGCTGGTGTCCACCGGCATCCG
CAAGGTGCTGTTCCTGGACGGCATCGACAAGGCCCAGGAGGAGCACGAGAAGTACCACTCCAACTGGCGCGCCATGGCCTCC
GACTTCAACCTGCCCCCCATCGTGGCCAAGGAGATCGTGGCCTCCTGCGACAAGTGCCAGCTGAAGGGCGAGGCCATGCACG
GCCAGGTGGACTGCTCCCCCGGCATCTGGCAGCTGGACTGCACCCACCTGGAGGGCAAGATCATCCTGGTGGCCGTGCACGT
GGCCTCCGGCTACATCGAGGCCGAGGTGATCCCCGCCGAGACCGGCCAGGAGACCGCCTACTTCATCCTGAAGCTGGCCGGC
CGCTGGCCCGTGAAGGTGATCCACACCGACAACGGCTCCAACTTCACCTCCGCCGCCGTGAAGGCCGCCTGCTGGTGGGCCG
GCATCCAGCAGGAGTTCGGCATCCCCTACAACCCCCAGTCCCAGGGCGTGGTGGAGTCCATGAACAAGGAGCTGAAGAAGAT
CATCGGCCAGGTGCGCGACCAGGCCGAGCACCTGAAGACCGCCGTGCAGATGGCCGTGTTCATCCACAACTTCAAGCGCAAG
GGCGGCATCGGCGGCTACTCCGCCGGCGAGCGCATCATCGACATCATCGCCACCGACATCCAGACCAAGGAGCTGCAGAAGC
AGATCACCAAGATCCAGAACTTCCGCGTGTACTACCGCGACTCCCGCGACCCCATCTGGAAGGGCCCCGCCAAGCTGCTGTG
GAAGGGCGAGGGCGCCGTGGTGATCCAGGACAACTCCGAGATCAAGGTGGTGCCCCGCCGCAAGGCCAAGATCATCCGCGAC
TACGGCAAGCAGATGGCCGGCGACGACTGCGTGGCCGGCCGCCAGGACGAGGACTAA

Fig. 108

A

62 2003_M GROUP anc pol.PEP

FFRENLAFQQGEAREFSSEQTRANSPTSRELRVRGGDNPLSEAGAERQGTVSFSFPQITLWQRPLVTIKIGGQLREALLDTG
ADDTVLEEINLPGKWKPKMIGGIGGFIKVRQYDQILIEICGKKAIGTVLVGPTPVNIIGRNMLTQIGCTLNFPISPIETVPV
KLKPGMDGPKVKQWPLTEEKIKALTEICTEMEKEGKISKIGPENPYNTPVFAIKKKDSTKWRKLVDFRELNKRTQDFWEVQL

GIPHPAGLKKKKSVTVLDVGDAYFSVPLDEDFRKYTAFTIPSINNETPGIRYQYNVLPQGWKGSPAIFQSSMTKILEPFRTK
NPEIVIYQYMDDLYVGSDLEIGQHRAKIEELREHLLRWGFTTPDKKHQKEPPFLWMGYELHPDKWTVQPIQLPEKDSWTVND
IQKLVGKLNWASQIYPGIKVKQLCKLLRGAKALTDIVPLTEEAELELAENREILKEPVHGVYYDPSKDLIAEIQKQGQDQWT
YQIYQEPFKNLKTGKYAKMRSAHTNDVKQLTEAVQKIATESIVIWGKTPKFRLPIQKETWETWWTEYWQATWIPEWEFVNTP
PLVKLWYQLEKEPIVGAETFYVDGAANRETKLGKAGYVTDRGRQKVVSLTETTNQKTELQAIHLALQDSGSEVNIVTDSQYA
LGIIQAQPDKSESELVNQIIEQLIKKEKVYLSWVPAHKGIGGNEQVDKLVSSGIRKVLFLDGIDKAQEEHEKYHSNWRAMAS
DFNLPPVVAKEIVASCDKCQLKGEAMHGQVDCSPGIWQLDCTHLEGKVILVAVHVASGYIEAEVIPAETGQETAYFILKLAG
RWPVKVIHTDNGSNFTSAAVKAACWWAGIQQEFGIPYNPQSQGVVESMNKELKKIIGQVRDQAEHLKTAVQMAVFIHNFKRK
GGIGGYSAGERIIDIIATDIQTKELQKQITKIQNFRVYYRDSRDPIWKGPAKLLWKGEGAVVIQDNSEIKVVPRRKAKIIRD
YGKQMAGDDCVAGRQDED$

2003_M.GROUP anc pol.OPT

TTCTTCCGCGAGAACCTGGCCTTCCAGCAGGGCGAGGCCCGCGAGTTCTCCTCCGAGCAGACCCGCGCCAACTCCCCCACCT
CCCGCGAGCTGCGCGTGCGCGGCGGCGACAACCCCCTGTCCGAGGCCGGCGCCGAGCGCCAGGGCACCGTGTCCTTCTCCTT
CCCCCAGATCACCCTGTGGCAGCGCCCCCTGGTGACCATCAAGATCGGCGGCCAGCTGCGCGAGGCCCTGCTGGACACCGGC
GCCGACGACACCGTGCTGGAGGAGATCAACCTGCCCGGCAAGTGGAAGCCCAAGATGATCGGCGGCATCGGCGGCTTCATCA
AGGTGCGCCAGTACGACCAGATCCTGATCGAGATCTGCGGCAAGAAGGCCATCGGCACCGTGCTGGTGGGCCCCACCCCCGT
GAACATCATCGGCCGCAACATGCTGACCCAGATCGGCTGCACCCTGAACTTCCCCATCTCCCCCATCGAGACCGTGCCCGTG
AAGCTGAAGCCCGGCATGGACGGCCCCAAGGTGAAGCAGTGGCCCCTGACCGAGGAGAAGATCAAGGCCCTGACCGAGATCT
GCACCGAGATGGAGAAGGAGGGCAAGATCTCCAAGATCGGCCCCGAGAACCCCTACAACACCCCCGTGTTCGCCATCAAGAA
GAAGGACTCCACCAAGTGGCGCAAGCTGGTGGACTTCCGCGAGCTGAACAAGCGCACCCAGGACTTCTGGGAGGTGCAGCTG
GGCATCCCCCACCCCGCCGGCCTGAAGAAGAAGAAGTCCGTGACCGTGCTGGACGTGGGCGACGCCTACTTCTCCGTGCCCC
TGGACGAGGACTTCCGCAAGTACACCGCCTTCACCATCCCCTCCATCAACAACGAGACCCCCGGCATCCGCTACCAGTACAA
CGTGCTGCCCCAGGGCTGGAAGGGCTCCCCCGCCATCTTCCAGTCCTCCATGACCAAGATCCTGGAGCCCTTCCGCACCAAG
AACCCCGAGATCGTGATCTACCAGTACATGGACGACCTGTACGTGGGCTCCGACCTGGAGATCGGCCAGCACCGCGCCAAGA
TCGAGGAGCTGCGCGAGCACCTGCTGCGCTGGGGCTTCACCACCCCCGACAAGAAGCACCAGAAGGAGCCCCCCTTCCTGTG
GATGGGCTACGAGCTGCACCCCGACAAGTGGACCGTGCAGCCCATCCAGCTGCCCGAGAAGGACTCCTGGACCGTGAACGAC
ATCCAGAAGCTGGTGGGCAAGCTGAACTGGGCCTCCCAGATCTACCCCGGCATCAAGGTGAAGCAGCTGTGCAAGCTGCTGC
GCGGCGCCAAGGCCCTGACCGACATCGTGCCCCTGACCGAGGAGGCCGAGCTGGAGCTGGCCGAGAACCGCGAGATCCTGAA
GGAGCCCGTGCACGGCGTGTACTACGACCCCTCCAAGGACCTGATCGCCGAGATCCAGAAGCAGGGCCAGGACCAGTGGACC
TACCAGATCTACCAGGAGCCCTTCAAGAACCTGAAGACCGGCAAGTACGCCAAGATGCGCTCCGCCCACACCAACGACGTGA
AGCAGCTGACCGAGGCCGTGCAGAAGATCGCCACCGAGTCCATCGTGATCTGGGGCAAGACCCCCAAGTTCCGCCTGCCCAT
CCAGAAGGAGACCTGGGAGACCTGGTGGACCGAGTACTGGCAGGCCACCTGGATCCCCGAGTGGGAGTTCGTGAACACCCCC
CCCCTGGTGAAGCTGTGGTACCAGCTGGAGAAGGAGCCCATCGTGGGCGCCGAGACCTTCTACGTGGACGGCGCCGCCAACC
GCGAGACCAAGCTGGGCAAGGCCGGCTACGTGACCGACCGCGGCCGCCAGAAGGTGGTGTCCCTGACCGAGACCACCAACCA
GAAGACCGAGCTGCAGGCCATCCACCTGGCCCTGCAGGACTCCGGCTCCGAGGTGAACATCGTGACCGACTCCCAGTACGCC
CTGGGCATCATCCAGGCCCAGCCCGACAAGTCCGAGTCCGAGCTGGTGAACCAGATCATCGAGCAGCTGATCAAGAAGGAGA
AGGTGTACCTGTCCTGGGTGCCCGCCCACAAGGGCATCGGCGGCAACGAGCAGGTGGACAAGCTGGTGTCCTCCGGCATCCG
CAAGGTGCTGTTCCTGGACGGCATCGACAAGGCCCAGGAGGAGCACGAGAAGTACCACTCCAACTGGCGCGCCATGGCCTCC
GACTTCAACCTGCCCCCCGTGGTGGCCAAGGAGATCGTGGCCTCCTGCGACAAGTGCCAGCTGAAGGGCGAGGCCATGCACG
GCCAGGTGGACTGCTCCCCCGGCATCTGGCAGCTGGACTGCACCCACCTGGAGGGCAAGGTGATCCTGGTGGCCGTGCACGT
GGCCTCCGGCTACATCGAGGCCGAGGTGATCCCCGCCGAGACCGGCCAGGAGACCGCCTACTTCATCCTGAAGCTGGCCGGC
CGCTGGCCCGTGAAGGTGATCCACACCGACAACGGCTCCAACTTCACCTCCGCCGCCGTGAAGGCCGCCTGCTGGTGGGCCG
GCATCCAGCAGGAGTTCGGCATCCCCTACAACCCCCAGTCCCAGGGCGTGGTGGAGTCCATGAACAAGGAGCTGAAGAAGAT
CATCGGCCAGGTGCGCGACCAGGCCGAGCACCTGAAGACCGCCGTGCAGATGGCCGTGTTCATCCACAACTTCAAGCGCAAG
GGCGGCATCGGCGGCTACTCCGCCGGCGAGCGCATCATCGACATCATCGCCACCGACATCCAGACCAAGGAGCTGCAGAAGC
AGATCACCAAGATCCAGAACTTCCGCGTGTACTACCGCGACTCCCGCGACCCCATCTGGAAGGGCCCCGCCAAGCTGCTGTG
GAAGGGCGAGGGCGCCGTGGTGATCCAGGACAACTCCGAGATCAAGGTGGTGCCCCGCCGCAAGGCCAAGATCATCCGCGAC
TACGGCAAGCAGATGGCCGGCGACGACTGCGTGGCCGGCCGCCAGGACGAGGACTAA

Fig. 109

63. 2003_CON_A1 pol.PEP

FFRENLAFQQGEARKFSSEQTGANSPTSRDLWDGGRDSLPSEAGAERQGTGPTFSFPQITLWQRPLVTVRIGGQLKEALLDT
GADDTVLEDINLPGKWKPKMIGGIGGFIKVKQYDQILIEICGKKAIGTVLVGPTPVNIIGRNMLTQIGCTLNFPISPIETVP
VKLKPGMDGPKVKQWPLTEEKIKALTEICTEMEKEGKISKIGPENPYNTPIFAIKKKDSTKWRKLVDFRELNKRTQDFWEVQ
LGIPHPAGLKKKKSVTVLDVGDAYFSVPLDESFRKYTAFTIPSTNNETPGIRYQYNVLPQGWKGSPAIFQSSMTKILEPFRS
KNPEIIIYQYMDDLYVGSDLEIGQHRTKIEELRAHLLSWGFTTPDKKHQKEPPFLWMGYELHPDKWTVQPIELPEKESWTVN
DIQKLVGKLNWASQIYAGIKVKQLCKLLRGAKALTDIVTLTEEAELELAENREILKDPVHGVYYDPSKDLIAEIQKQGQDQW
TYQIYQEPFKNLKTGKYARKRSAHTNDVKQLAEVVQKVVMESIVIWGKTPKFKLPIQKETWETWWMDYWQATWIPEWEFVNT
PPLVKLWYQLEKDPIVGAETFYVDGAANRETKLGKAGYVTDRGRQKVVSLTETTNQKTELHAIHLALQDSGSEVNIVTDSQY

ALGIIQAQPDRSESELVNQIIEKLIGKDKVYLSWVPAHKGIGGNEQVDKLVSSGIRKVLFLDGIDKAQEEHERYHSNWRAMA
SDFNLPPIVAKEIVASCDKCQLKGEAMHGQVDCSPGIWQLDCTHLEGKVILVAVHVASGYIEAEVIPAETGQETAYFLLKLA
GRWPVKVVHTDNGSNFTSAAVKAACWWANIQQEFGIPYNPQSQGVVESMNKELKKIIGQVREQAEHLKTAVQMAVFIHNFKR
KGGIGGYSAGERIIDIIATDIQTKELQKQITKIQNFRVYYRDSRDPIWKGPAKLLWKGEGAVVIQDNSDIKVVPRRKAKIIR
DYGKQMAGDDCVAGRQDED$

2003_CON_A1 pol.OPT

TTCTTCCGCGAGAACCTGGCCTTCCAGCAGGGCGAGGCCCGCAAGTTCTCCTCCGAGCAGACCGGCGCCAACTCCCCCACCT
CCCGCGACCTGTGGGACGGCGGCCGCGACTCCCTGCCCTCCGAGGCCGGCGCCGAGCGCCAGGGCACCGGCCCCACCTTCTC
CTTCCCCCAGATCACCCTGTGGCAGCGCCCCCTGGTGACCGTGCGCATCGGCGGCCAGCTGAAGGAGGCCCTGCTGGACACC
GGCGCCGACGACACCGTGCTGGAGGACATCAACCTGCCCGGCAAGTGGAAGCCCAAGATGATCGGCGGCATCGGCGGCTTCA
TCAAGGTGAAGCAGTACGACCAGATCCTGATCGAGATCTGCGGCAAGAAGGCCATCGGCACCGTGCTGGTGGGCCCCACCCC
CGTGAACATCATCGGCCGCAACATGCTGACCCAGATCGGCTGCACCCTGAACTTCCCCATCTCCCCCATCGAGACCGTGCCC
GTGAAGCTGAAGCCCGGCATGGACGGCCCCAAGGTGAAGCAGTGGCCCCTGACCGAGGAGAAGATCAAGGCCCTGACCGAGA
TCTGCACCGAGATGGAGAAGGAGGGCAAGATCTCCAAGATCGGCCCCGAGAACCCCTACAACACCCCCATCTTCGCCATCAA
GAAGAAGGACTCCACCAAGTGGCGCAAGCTGGTGGACTTCCGCGAGCTGAACAAGCGCACCCAGGACTTCTGGGAGGTGCAG
CTGGGCATCCCCCACCCCGCCGGCCTGAAGAAGAAGAAGTCCGTGACCGTGCTGGACGTGGGCGACGCCTACTTCTCCGTGC
CCCTGGACGAGTCCTTCCGCAAGTACACCGCCTTCACCATCCCCTCCACCAACAACGAGACCCCCGGCATCCGCTACCAGTA
CAACGTGCTGCCCCAGGGCTGGAAGGGCTCCCCCGCCATCTTCCAGTCCTCCATGACCAAGATCCTGGAGCCCTTCCGCTCC
AAGAACCCCGAGATCATCATCTACCAGTACATGGACGACCTGTACGTGGGCTCCGACCTGGAGATCGGCCAGCACCGCACCA
AGATCGAGGAGCTGCGCGCCCACCTGCTGTCCTGGGGCTTCACCACCCCCGACAAGAAGCACCAGAAGGAGCCCCCCTTCCT
GTGGATGGGCTACGAGCTGCACCCCGACAAGTGGACCGTGCAGCCCATCGAGCTGCCCGAGAAGGAGTCCTGGACCGTGAAC
GACATCCAGAAGCTGGTGGGCAAGCTGAACTGGGCCTCCCAGATCTACGCCGGCATCAAGGTGAAGCAGCTGTGCAAGCTGC
TGCGCGGCGCCAAGGCCCTGACCGACATCGTGACCCTGACCGAGGAGGCCGAGCTGGAGCTGGCCGAGAACCGCGAGATCCT
GAAGGACCCCGTGCACGGCGTGTACTACGACCCCTCCAAGGACCTGATCGCCGAGATCCAGAAGCAGGGCCAGGACCAGTGG
ACCTACCAGATCTACCAGGAGCCCTTCAAGAACCTGAAGACCGGCAAGTACGCCCGCAAGCGCTCCGCCCACACCAACGACG
TGAAGCAGCTGGCCGAGGTGGTGCAGAAGGTGGTGATGGAGTCCATCGTGATCTGGGGCAAGACCCCCAAGTTCAAGCTGCC
CATCCAGAAGGAGACCTGGGAGACCTGGTGGATGGACTACTGGCAGGCCACCTGGATCCCCGAGTGGGAGTTCGTGAACACC
CCCCCCCTGGTGAAGCTGTGGTACCAGCTGGAGAAGGACCCCATCGTGGGCGCCGAGACCTTCTACGTGGACGGCGCCGCCA
ACCGCGAGACCAAGCTGGGCAAGGCCGGCTACGTGACCGACCGCGGCCGCCAGAAGGTGGTGTCCCTGACCGAGACCACCAA
CCAGAAGACCGAGCTGCACGCCATCCACCTGGCCCTGCAGGACTCCGGCTCCGAGGTGAACATCGTGACCGACTCCCAGTAC
GCCCTGGGCATCATCCAGGCCCAGCCCGACCGCTCCGAGTCCGAGCTGGTGAACCAGATCATCGAGAAGCTGATCGGCAAGG
ACAAGGTGTACCTGTCCTGGGTGCCCGCCCACAAGGGCATCGGCGGCAACGAGCAGGTGGACAAGCTGGTGTCCTCCGGCAT
CCGCAAGGTGCTGTTCCTGGACGGCATCGACAAGGCCCAGGAGGAGCACGAGCGCTACCACTCCAACTGGCGCGCCATGGCC
TCCGACTTCAACCTGCCCCCCATCGTGGCCAAGGAGATCGTGGCCTCCTGCGACAAGTGCCAGCTGAAGGGCGAGGCCATGC
ACGGCCAGGTGGACTGCTCCCCCGGCATCTGGCAGCTGGACTGCACCCACCTGGAGGGCAAGGTGATCCTGGTGGCCGTGCA
CGTGGCCTCCGGCTACATCGAGGCCGAGGTGATCCCCGCCGAGACCGGCCAGGAGACCGCCTACTTCCTGCTGAAGCTGGCC
GGCCGCTGGCCCGTGAAGGTGGTGCACACCGACAACGGCTCCAACTTCACCTCCGCCGCCGTGAAGGCCGCCTGCTGGTGGG
CCAACATCCAGCAGGAGTTCGGCATCCCCTACAACCCCCAGTCCCAGGGCGTGGTGGAGTCCATGAACAAGGAGCTGAAGAA
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64. 2003_A1.anc pol.PEP

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65. 2003_CON_A2 pol.PEP

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67. 2003_B.anc pol.PEP

FFRENLAFPQGKAREFSSEQTRANSPTRRELQVWGRDNNPLSEAGADRQGTVSFSFPQITLWQRPLVTIKIGGQLKEALLDT
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TCCGACTTCAACCTGCCCCCCGTGGTGGCCAAGGAGATCGTGGCCTCCTGCGACAAGTGCCAGCTGAAGGGCGAGGCCATGC
ACGGCCAGGTGGACTGCTCCCCCGGCATCTGGCAGCTGGACTGCACCCACCTGGAGGGCAAGATCATCCTGGTGGCCGTGCA
CGTGGCCTCCGGCTACATCGAGGCCGAGGTGATCCCCGCCGAGACCGGCCAGGAGACCGCCTACTTCATCCTGAAGCTGGCC
GGCCGCTGGCCCGTGAAGGTGATCCACACCGACAACGGCTCCAACTTCACCTCCACCACCGTGAAGGCCGCCTGCTGGTGGG
CCGGCATCAAGCAGGAGTTCGGCATCCCCTACAACCCCCAGTCCCAGGGCGTGGTGGAGTCCATGAACAAGGAGCTGAAGAA
GATCATCGGCCAGGTGCGCGACCAGGCCGAGCACCTGAAGACCGCCGTGCAGATGGCCGTGTTCATCCACAACTTCAAGCGC
AAGGGCGGCATCGGCGGCTACTCCGCCGGCGAGCGCATCGTGGACATCATCGCCACCGACATCCAGACCAAGGAGCTGCAGA
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GTGGAAGGGCGAGGGCGCCGTGGTGATCCAGGACAACTCCGACATCAAGGTGGTGCCCCGCCGCAAGGCCAAGATCATCCGC
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7.112

68. 2003_CON_C pol.PEP

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FFRENLAFPQGEAREFPSEQTRANSPTSRELQVRGDNPRSEAGAERQGTLNFPQITLWQRPLVSIKVGGQIKEALLDTGADD
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PGMDGPKVKQWPLTEEKIKALTAICEEMEKEGKITKIGPENPYNTPVFAIKKKDSTKWRKLVDFRELNKRTQDFWEVQLGIP
HPAGLKKKKSVTVLDVGDAYFSVPLDEGFRKYTAFTIPSINNETPGIRYQYNVLPQGWKGSPAIFQSSMTKILEPFRAQNPE
IVIYQYMDDLYVGSDLEIGQHRAKIEELREHLLKWGFTTPDKKHQKEPPFLWMGYELHPDKWTVQPIQLPEKDSWTVNDIQK
LVGKLNWASQIYPGIKVRQLCKLLRGAKALTDIVPLTEEAELELAENREILKEPVHGVYYDPSKDLIAEIQKQGHDQWTYQI
YQEPFKNLKTGKYAKMRTAHTNDVKQLTEAVQKIAMESIVIWGKTPKFRLPIQKETWETWWTDYWQATWIPEWEFVNTPPLV
KLWYQLEKEPIAGAETFYVDGAANRETKIGKAGYVTDRGRQKIVSLTETTNQKTELQAIQLALQDSGSEVNIVTDSQYALGI
IQAQPDKSESELVNQIIEQLIKKERVYLSWVPAHKGIGGNEQVDKLVSSGIRKVLFLDGIDKAQEEHEKYHSNWRAMASEFN
LPPIVAKEIVASCDKCQLKGEAIHGQVDCSPGIWQLDCTHLEGKIILVAVHVASGYIEAEVIPAETGQETAYYILKLAGRWP
VKVIHTDNGSNFTSAAVKAACWWAGIQQEFGIPYNPQSQGVVESMNKELKKIIGQVRDQAEHLKTAVQMAVFIHNFKRKGGI
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2003_CON_C pol.OPT

B

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CACCCTGTGGCAGCGCCCCCTGGTGTCCATCAAGGTGGGCGGCCAGATCAAGGAGGCCCTGCTGGACACCGGCGCCGACGAC
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AGTACGACCAGATCCTGATCGAGATCTGCGGCAAGAAGGCCATCGGCACCGTGCTGGTGGGCCCCACCCCCGTGAACATCAT
CGGCCGCAACATGCTGACCCAGCTGGGCTGCACCCTGAACTTCCCCATCTCCCCCATCGAGACCGTGCCCGTGAAGCTGAAG
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69. 2003_C.anc pol.PEP

FFRENLAFPQGEAREFPSEQTRANSPTSRELQVGRDNPRSEAGAERQGTLTLNFPQITLWQRPLVSIKVGGQIKEALLDTGA
DDTVLEEINLPGKWKPKMIGGIGGFIKVRQYDQILIEICGKKAIGTVLVGPTPVNIIGRNMLTQLGCTLNFPISPIETVPVK
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IPHPAGLKKKKSVTVLDVGDAYFSVPLDEGFRKYTAFTIPSINNETPGIRYQYNVLPQGWKGSPAIFQSSMTKILEPFRAQN
PEIVIYQYMDDLYVGSDLEIGQHRAKIEELREHLLKWGFTTPDKKHQKEPPFLWMGYELHPDKWTVQPIQLPEKDSWTVNDI
QKLVGKLNWASQIYPGIKVRQLCKLLRGAKALTDIVPLTEEAELELAENREILKEPVHGVYYDPSKDLIAEIQKQGHDQWTY
QIYQEPFKNLKTGKYAKMRTAHTNDVKQLTEAVQKIAMESIVIWGKTPKFRLPIQKETWETWWTDYWQATWIPEWEFVNTPP
LVKLWYQLEKEPIAGAETFYVDGAANRETKIGKAGYVTDRGRQKIVSLTETTNQKTELQAIQLALQDSGSEVNIVTDSQYAL
GIIQAQPDKSESELVNQIIEQLIKKEKVYLSWVPAHKGIGGNEQVDKLVSSGIRKVLFLDGIDKAQEEHEKYHSNWRAMASE
FNLPPIVAKEIVASCDKCQLKGEAMHGQVDCSPGIWQLDCTHLEGKIILVAVHVASGYIEAEVIPAETGQETAYFILKLAGR
WPVKVIHTDNGSNFTSAAVKAACWWAGIQQEFGIPYNPQSQGVVESMNKELKKIIGQVRDQAEHLKTAVQMAVFIHNFKRKG
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3.13 A

70. 2003_CON_D pol.PEP
FFRENLAFPQGKAGELSSEQTRANSPTSRELRVWGGDNPLSETGAERQGTVSFNFPQITLWQRPLVTIKIGGQLKEALLDTG
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GIPHPAGLKKKKSVTVLDVGDAYFSVPLDEDFRKYTAFTIPSINNETPGIRYQYNVLPQGWKGSPAIFQSSMTKILEPFRKQ
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IQKLVGKLNWASQIYPGIKVRQLCKLLRGTKALTEVIPLTEEAELELAENREILKEPVHGVYYDPSKDLIAEIQKQGQGQWT
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PLVKLWYQLEKEPIIGAETFYVDGAANRETKLGKAGYVTDRGRQKVVPLTDTTNQKTELQAINLALQDSGLEVNIVTDSQYA
LGIIQAQPDKSESELVSQIIEQLIKKEKVYLAWVPAHKGIGGNEQVDKLVSNGIRKVLFLDGIDKAQEEHEKYHNNWRAMAS
DFNLPPVVAKEIVASCDKCQLKGEAMHGQVDCSPGIWQLDCTHLEGKVILVAVHVASGYIEAEVIPAETGQETAYFLLKLAG
RWPVKVVHTDNGSNFTSAAVKAACWWAGIKQEFGIPYNPQSQGVVESMNKELKKIIGQVRDQAEHLKTAVQMAVFIHNFKRK
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YGKQMAGDDCVASRQDED$

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2003_CON_D pol.OPT
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71. 2003_CON_F1 pol.PEP

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VKLKPGMDGPKVKQWPLTEEKIKALTEICTEMEKEGKISKIGPENPYNTPVFAIKKKDSTKWRKLVDFRELNKRTQDFWEVQ
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PPLVKLWYQLETEPIVGAETFYVDGASNRETKKGKAGYVTDRGRQKVVSLTETTNQKAELQAIHLALQDSGSEVNIVTDSQY
ALGIIQAQPDKSESELVNQIIEQLIQKEKVYLSWVPAHKGIGGNEQVDKLVSAGIRKILFLDGIDKAQEEHEKYHNNWRAMA
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CATCCTGAAGGAGACCTGGGACACCTGGTGGACCGACTACTGGCAGGCCACCTGGATCCCCGAGTGGGAGTTCGTGAACACC
CCCCCCCTGGTGAAGCTGTGGTACCAGCTGGAGACCGAGCCCATCGTGGGCGCCGAGACCTTCTACGTGGACGGCGCCTCCA
ACCGCGAGACCAAGAAGGGCAAGGCCGGCTACGTGACCGACCGCGGCCGCCAGAAGGTGGTGTCCCTGACCGAGACCACCAA
CCAGAAGGCCGAGCTGCAGGCCATCCACCTGGCCCTGCAGGACTCCGGCTCCGAGGTGAACATCGTGACCGACTCCCAGTAC
GCCCTGGGCATCATCCAGGCCCAGCCCGACAAGTCCGAGTCCGAGCTGGTGAACCAGATCATCGAGCAGCTGATCCAGAAGG
AGAAGGTGTACCTGTCCTGGGTGCCCGCCCACAAGGGCATCGGCGGCAACGAGCAGGTGGACAAGCTGGTGTCCGCCGGCAT
CCGCAAGATCCTGTTCCTGGACGGCATCGACAAGGCCCAGGAGGAGCACGAGAAGTACCACAACAACTGGCGCGCCATGGCC
TCCGACTTCAACCTGCCCCCCGTGGTGGCCAAGGAGATCGTGGCCTCCTGCGACAAGTGCCAGCTGAAGGGCGAGGCCATGC
ACGGCCAGGTGGACTGCTCCCCCGGCATCTGGCAGCTGGACTGCACCCACCTGGAGGGCAAGATCATCCTGGTGGCCGTGCA
CGTGGCCTCCGGCTACATCGAGGCCGAGGTGATCCCCGCCGAGACCGGCCAGGAGACCGCCTACTTCATCCTGAAGCTGGCC
GGCCGCTGGCCCGTGAAGATCATCCACACCGACAACGGCTCCAACTTCACCTCCGCCGCCGTGAAGGCCGCCTGCTGGTGGG
CCGGCATCCAGCAGGAGTTCGGCATCCCCTACAACCCCCAGTCCCAGGGCGTGGTGGAGTCCATGAACAAGGAGCTGAAGAA
GATCATCGGCCAGGTGCGCGACCAGGCCGAGCACCTGAAGACCGCCGTGCAGATGGCCGTGTTCATCCACAACTTCAAGCGC

AAGGGCGGCATCGGCGGCTACTCCGCCGGCGAGCGCATCATCGACATCATCGCCACCGACATCCAGACCCGCGAGCTGCAGA
AGCAGATCACCAAGATCCAGAACTTCCGCGTGTACTACCGCGACTCCCGCGACCCCGTGTGGAAGGGCCCCGCCAAGCTGCT
GTGGAAGGGCGAGGGCGCCGTGGTGATCCAGGACAACTCCGAGATCAAGGTGGTGCCCCGCCGCAAGGCCAAGATCATCCGC
GACTACGGCAAGCAGATGGCCGGCGACGACTGCGTGGCCGGCCGCCAGGACGAGGACTAA

3.115 A

72. 2003_CON_F2 pol.PEP

FFRENLAFQQGEARKFSSEQTRANSPASRELRVRRGDNSLPEAGAERQGTGSSLDFPQITLWQRPLVTIKVGGQLREALLDT
GADDTVLEDINLPGKWKPKMIGGIGGFIKVRQYDQIPIEICGQKAIGTVLVGPTPVNIIGRNMLTQIGCTLNFPISPIETVP
VKLKPGMDGPKVKQWPLTEEKIKALTEICTEMEKEGKISKIGPENPYNTPVFAIKKKDSTKWRKLVDFRELNKRTQDFWEVQ
LGIPHPAGLKKKKSVTVLDVGDAYFSVPLDKEFRKYTAFTIPSINNETPGIRYQYNVLPQGWKGSPAIFQSSMTKILEPFRA
KNPEIVIYQYMDDLYVGSDLEIGQHRTKIEELREHLLRWGFTTPDKKHQKEPPFLWMGYELHPDKWTVQAIQLPDKSSWTVN
DIQKLVGKLNWASQIYPGIRVKHLCKLLRGAKALTDVVPLTAEAELELAENREILKEPVHGVYYDPSKDLIAEIQKQGHDQW
TYQIYQEPHKNLKTGKYARRKSAHTNDVKQLTEVVQKIATEGIVIWGKVPKFRLPIQKETWEIWWTEYWQATWIPEWEFVNT
PPLVKLWYQLETEPIVGAETFYVDGAANRETKLGKAGYVTDRGRQKVVPLTETTNQKTELQAIHLALQDSGSEVNIVTDSQY
ALGIIQAHPDKSESELVNQIIEQLIQKERVYLSWVPAHKGIGGNEQVDKLVSTGIRKVLFLDGIDKAQEEHEKYHSNWRAMA
SDFNLPPVVAKEIVASCDKCQLKGEAMHGQVDCSPGIWQLDCTHLEGKIILVAVHVASGYIEAEVIPAETGQETAYFILKLA
GRWPVKIIHTDNGSNFTSTVVKAACWWAGIQQEFGIPYNPQSQGVVESMNKELKKIIGQVRDQAEHLKTAVQMAVFIHNFKR
KGGIGGYSAGERIIDIIATDIQTKELQKQITKIQNFRVYFRDSRDPVWKGPAKLLWKGEGAVVIQDNNEIKVVPRRKAKIIR
DYGKQMAGDDCVAGRQDED$

2003_CON_F2 pol.OPT

3

TTCTTCCGCGAGAACCTGGCCTTCCAGCAGGGCGAGGCCCGCAAGTTCTCCTCCGAGCAGACCCGCGCCAACTCCCCCGCCT
CCCGCGAGCTGCGCGTGCGCCGCGGCGACAACTCCCTGCCCGAGGCCGGCGCCGAGCGCCAGGGCACCGGCTCCTCCCTGGA
CTTCCCCCAGATCACCCTGTGGCAGCGCCCCCTGGTGACCATCAAGGTGGGCGGCCAGCTGCGCGAGGCCCTGCTGGACACC
GGCGCCGACGACACCGTGCTGGAGGACATCAACCTGCCCGGCAAGTGGAAGCCCAAGATGATCGGCGGCATCGGCGGCTTCA
TCAAGGTGCGCCAGTACGACCAGATCCCCATCGAGATCTGCGGCCAGAAGGCCATCGGCACCGTGCTGGTGGGCCCCACCCC
CGTGAACATCATCGGCCGCAACATGCTGACCCAGATCGGCTGCACCCTGAACTTCCCCATCTCCCCCATCGAGACCGTGCCC
GTGAAGCTGAAGCCCGGCATGGACGGCCCCAAGGTGAAGCAGTGGCCCCTGACCGAGGAGAAGATCAAGGCCCTGACCGAGA
TCTGCACCGAGATGGAGAAGGAGGGCAAGATCTCCAAGATCGGCCCCGAGAACCCCTACAACACCCCCGTGTTCGCCATCAA
GAAGAAGGACTCCACCAAGTGGCGCAAGCTGGTGGACTTCCGCGAGCTGAACAAGCGCACCCAGGACTTCTGGGAGGTGCAG
CTGGGCATCCCCCACCCCGCCGGCCTGAAGAAGAAGAAGTCCGTGACCGTGCTGGACGTGGGCGACGCCTACTTCTCCGTGC
CCCTGGACAAGGAGTTCCGCAAGTACACCGCCTTCACCATCCCCTCCATCAACAACGAGACCCCCGGCATCCGCTACCAGTA
CAACGTGCTGCCCCAGGGCTGGAAGGGCTCCCCCGCCATCTTCCAGTCCTCCATGACCAAGATCCTGGAGCCCTTCCGCGCC
AAGAACCCCGAGATCGTGATCTACCAGTACATGGACGACCTGTACGTGGGCTCCGACCTGGAGATCGGCCAGCACCGCACCA
AGATCGAGGAGCTGCGCGAGCACCTGCTGCGCTGGGGCTTCACCACCCCCGACAAGAAGCACCAGAAGGAGCCCCCCTTCCT
GTGGATGGGCTACGAGCTGCACCCCGACAAGTGGACCGTGCAGGCCATCCAGCTGCCCGACAAGTCCTCCTGGACCGTGAAC
GACATCCAGAAGCTGGTGGGCAAGCTGAACTGGGCCTCCCAGATCTACCCCGGCATCCGCGTGAAGCACCTGTGCAAGCTGC
TGCGCGGCGCCAAGGCCCTGACCGACGTGGTGCCCCTGACCGCCGAGGCCGAGCTGGAGCTGGCCGAGAACCGCGAGATCCT
GAAGGAGCCCGTGCACGGCGTGTACTACGACCCCTCCAAGGACCTGATCGCCGAGATCCAGAAGCAGGGCCACGACCAGTGG
ACCTACCAGATCTACCAGGAGCCCCACAAGAACCTGAAGACCGGCAAGTACGCCCGCCGCAAGTCCGCCCACACCAACGACG
TGAAGCAGCTGACCGAGGTGGTGCAGAAGATCGCCACCGAGGGCATCGTGATCTGGGGCAAGGTGCCCAAGTTCCGCCTGCC
CATCCAGAAGGAGACCTGGGAGATCTGGTGGACCGAGTACTGGCAGGCCACCTGGATCCCCGAGTGGGAGTTCGTGAACACC
CCCCCCCTGGTGAAGCTGTGGTACCAGCTGGAGACCGAGCCCATCGTGGGCGCCGAGACCTTCTACGTGGACGGCGCCGCCA
ACCGCGAGACCAAGCTGGGCAAGGCCGGCTACGTGACCGACCGCGGCCGCCAGAAGGTGGTGCCCCTGACCGAGACCACCAA
CCAGAAGACCGAGCTGCAGGCCATCCACCTGGCCCTGCAGGACTCCGGCTCCGAGGTGAACATCGTGACCGACTCCCAGTAC
GCCCTGGGCATCATCCAGGCCCACCCCGACAAGTCCGAGTCCGAGCTGGTGAACCAGATCATCGAGCAGCTGATCCAGAAGG
AGCGCGTGTACCTGTCCTGGGTGCCCGCCCACAAGGGCATCGGCGGCAACGAGCAGGTGGACAAGCTGGTGTCCACCGGCAT
CCGCAAGGTGCTGTTCCTGGACGGCATCGACAAGGCCCAGGAGGAGCACGAGAAGTACCACTCCAACTGGCGCGCCATGGCC
TCCGACTTCAACCTGCCCCCCGTGGTGGCCAAGGAGATCGTGGCCTCCTGCGACAAGTGCCAGCTGAAGGGCGAGGCCATGC
ACGGCCAGGTGGACTGCTCCCCCGGCATCTGGCAGCTGGACTGCACCCACCTGGAGGGCAAGATCATCCTGGTGGCCGTGCA
CGTGGCCTCCGGCTACATCGAGGCCGAGGTGATCCCCGCCGAGACCGGCCAGGAGACCGCCTACTTCATCCTGAAGCTGGCC
GGCCGCTGGCCCGTGAAGATCATCCACACCGACAACGGCTCCAACTTCACCTCCACCGTGGTGAAGGCCGCCTGCTGGTGGG
CCGGCATCCAGCAGGAGTTCGGCATCCCCTACAACCCCCAGTCCCAGGGCGTGGTGGAGTCCATGAACAAGGAGCTGAAGAA
GATCATCGGCCAGGTGCGCGACCAGGCCGAGCACCTGAAGACCGCCGTGCAGATGGCCGTGTTCATCCACAACTTCAAGCGC
AAGGGCGGCATCGGCGGCTACTCCGCCGGCGAGCGCATCATCGACATCATCGCCACCGACATCCAGACCAAGGAGCTGCAGA
AGCAGATCACCAAGATCCAGAACTTCCGCGTGTACTTCCGCGACTCCCGCGACCCCGTGTGGAAGGGCCCCGCCAAGCTGCT
GTGGAAGGGCGAGGGCGCCGTGGTGATCCAGGACAACAACGAGATCAAGGTGGTGCCCCGCCGCAAGGCCAAGATCATCCGC
GACTACGGCAAGCAGATGGCCGGCGACGACTGCGTGGCCGGCCGCCAGGACGAGGACTAA

Fig. 116

A

73. 2003_CON_G pol.PEP

FFRENLAFQQGEAREFSSEQARANSPTRRELRVRRGDSPLPEAGAEGKGAISLSFPQITLWQRPLVTVKIGGQLIEALLDTG
ADDTVLEEINLPGKWKPKMIGGIGGFIKVRQYDQILIEISGKKAIGTVLVGPTPINIIGRNMLTQIGCTLNFPISPIETVPV
KLKPGMDGPKVKQWPLTEEKIKALTEICTEMEKEGKISKIGPENPYNTPIFAIKKKDSTKWRKLVDFRELNKRTQDFWEVQL
GIPHPAGLKKKKSVTVLDVGDAYFSVPLDENFRKYTAFTIPSTNNETPGIRYQYNVLPQGWKGSPAIFQSSMTKILEPFRTK
NPEIVIYQYMDDLYVGSDLEIGQHRAKIEELREHLLRWGFTTPDKKHQKEPPFLWMGYELHPDKWTVQPIQLPDKESWTVND
IQKLVGKLNWASQIYPGIKVKQLCKLLRGAKALTDIVPLTAEAELELAENREILKEPVHGVYYDPSKELIAEVQKQGLDQWT
YQIYQEPYKNLKTGKYAKRGSAHTNDVKQLTEVVQKIATESIVIWGKTPKFKLPIRKETWEVWWTEYWQATWIPEWEFVNTP
PLVKLWYRLETEPIPGAETYYVDGAANRETKLGKAGYVTDKGKQKIITLTETTNQKAELQAIHLALQDSGSEVNIVTDSQYA
LGIIQAQPDRSESELVNQIIEQLIKKEKVYLSWVPAHKGIGGNEQVDKLVSSGIRKVLFLDGIDKAQEEHERYHSNWRAMAS
DFNLPPIVAKEIVASCDKCQLKGEAMHGQVDCSPGIWQLDCTHLEGKIILVAVHVASGYIEAEVIPAETGQETAYFILKLAG
RWPVKVIHTDNGSNFTSAAVKAACWWANITQEFGIPYNPQSQGVVESMNKELKKIIGQVRDQAEHLKTAVQMAVFIHNFKRK
GGIGGYSAGERIIDIIASDIQTKELQKQITKIQNFRVYYRDSRDPIWKGPAKLLWKGEGAVVIQDNNEIKVVPRRKAKIIRD
YGKQMAGDDCVAGRQDED$

B

2003_CON_G pol.OPT

TTCTTCCGCGAGAACCTGGCCTTCCAGCAGGGCGAGGCCCGCGAGTTCTCCTCCGAGCAGGCCCGCGCCAACTCCCCCACCC
GCCGCGAGCTGCGCGTGCGCCGCGGCGACTCCCCCCTGCCCGAGGCCGGCGCCGAGGGCAAGGGCGCCATCTCCCTGTCCTT
CCCCCAGATCACCCTGTGGCAGCGCCCCCTGGTGACCGTGAAGATCGGCGGCCAGCTGATCGAGGCCCTGCTGGACACCGGC
GCCGACGACACCGTGCTGGAGGAGATCAACCTGCCCGGCAAGTGGAAGCCCAAGATGATCGGCGGCATCGGCGGCTTCATCA
AGGTGCGCCAGTACGACCAGATCCTGATCGAGATCTCCGGCAAGAAGGCCATCGGCACCGTGCTGGTGGGCCCCACCCCCAT
CAACATCATCGGCCGCAACATGCTGACCCAGATCGGCTGCACCCTGAACTTCCCCATCTCCCCCATCGAGACCGTGCCCGTG
AAGCTGAAGCCCGGCATGGACGGCCCCAAGGTGAAGCAGTGGCCCCTGACCGAGGAGAAGATCAAGGCCCTGACCGAGATCT
GCACCGAGATGGAGAAGGAGGGCAAGATCTCCAAGATCGGCCCCGAGAACCCCTACAACACCCCCATCTTCGCCATCAAGAA
GAAGGACTCCACCAAGTGGCGCAAGCTGGTGGACTTCCGCGAGCTGAACAAGCGCACCCAGGACTTCTGGGAGGTGCAGCTG
GGCATCCCCCACCCCGCCGGCCTGAAGAAGAAGAAGTCCGTGACCGTGCTGGACGTGGGCGACGCCTACTTCTCCGTGCCCC
TGGACGAGAACTTCCGCAAGTACACCGCCTTCACCATCCCCTCCACCAACAACGAGACCCCCGGCATCCGCTACCAGTACAA
CGTGCTGCCCCAGGGCTGGAAGGGCTCCCCCGCCATCTTCCAGTCCTCCATGACCAAGATCCTGGAGCCCTTCCGCACCAAG
AACCCCGAGATCGTGATCTACCAGTACATGGACGACCTGTACGTGGGCTCCGACCTGGAGATCGGCCAGCACCGCGCCAAGA
TCGAGGAGCTGCGCGAGCACCTGCTGCGCTGGGGCTTCACCACCCCCGACAAGAAGCACCAGAAGGAGCCCCCCTTCCTGTG
GATGGGCTACGAGCTGCACCCCGACAAGTGGACCGTGCAGCCCATCCAGCTGCCCGACAAGGAGTCCTGGACCGTGAACGAC
ATCCAGAAGCTGGTGGGCAAGCTGAACTGGGCCTCCCAGATCTACCCCGGCATCAAGGTGAAGCAGCTGTGCAAGCTGCTGC
GCGGCGCCAAGGCCCTGACCGACATCGTGCCCCTGACCGCCGAGGCCGAGCTGGAGCTGGCCGAGAACCGCGAGATCCTGAA
GGAGCCCGTGCACGGCGTGTACTACGACCCCTCCAAGGAGCTGATCGCCGAGGTGCAGAAGCAGGGCCTGGACCAGTGGACC
TACCAGATCTACCAGGAGCCCTACAAGAACCTGAAGACCGGCAAGTACGCCAAGCGCGGCTCCGCCCACACCAACGACGTGA
AGCAGCTGACCGAGGTGGTGCAGAAGATCGCCACCGAGTCCATCGTGATCTGGGGCAAGACCCCCAAGTTCAAGCTGCCCAT
CCGCAAGGAGACCTGGGAGGTGTGGTGGACCGAGTACTGGCAGGCCACCTGGATCCCCGAGTGGGAGTTCGTGAACACCCCC
CCCCTGGTGAAGCTGTGGTACCGCCTGGAGACCGAGCCCATCCCCGGCGCCGAGACCTACTACGTGGACGGCGCCGCCAACC
GCGAGACCAAGCTGGGCAAGGCCGGCTACGTGACCGACAAGGGCAAGCAGAAGATCATCACCCTGACCGAGACCACCAACCA
GAAGGCCGAGCTGCAGGCCATCCACCTGGCCCTGCAGGACTCCGGCTCCGAGGTGAACATCGTGACCGACTCCCAGTACGCC
CTGGGCATCATCCAGGCCCAGCCCGACCGCTCCGAGTCCGAGCTGGTGAACCAGATCATCGAGCAGCTGATCAAGAAGGAGA
AGGTGTACCTGTCCTGGGTGCCCGCCCACAAGGGCATCGGCGGCAACGAGCAGGTGGACAAGCTGGTGTCCTCCGGCATCCG
CAAGGTGCTGTTCCTGGACGGCATCGACAAGGCCCAGGAGGAGCACGAGCGCTACCACTCCAACTGGCGCGCCATGGCCTCC
GACTTCAACCTGCCCCCCATCGTGGCCAAGGAGATCGTGGCCTCCTGCGACAAGTGCCAGCTGAAGGGCGAGGCCATGCACG
GCCAGGTGGACTGCTCCCCCGGCATCTGGCAGCTGGACTGCACCCACCTGGAGGGCAAGATCATCCTGGTGGCCGTGCACGT
GGCCTCCGGCTACATCGAGGCCGAGGTGATCCCCGCCGAGACCGGCCAGGAGACCGCCTACTTCATCCTGAAGCTGGCCGGC
CGCTGGCCCGTGAAGGTGATCCACACCGACAACGGCTCCAACTTCACCTCCGCCGCCGTGAAGGCCGCCTGCTGGTGGGCCA
ACATCACCCAGGAGTTCGGCATCCCCTACAACCCCCAGTCCCAGGGCGTGGTGGAGTCCATGAACAAGGAGCTGAAGAAGAT
CATCGGCCAGGTGCGCGACCAGGCCGAGCACCTGAAGACCGCCGTGCAGATGGCCGTGTTCATCCACAACTTCAAGCGCAAG
GGCGGCATCGGCGGCTACTCCGCCGGCGAGCGCATCATCGACATCATCGCCTCCGACATCCAGACCAAGGAGCTGCAGAAGC
AGATCACCAAGATCCAGAACTTCCGCGTGTACTACCGCGACTCCCGCGACCCCATCTGGAAGGGCCCCGCCAAGCTGCTGTG
GAAGGGCGAGGGCGCCGTGGTGATCCAGGACAACAACGAGATCAAGGTGGTGCCCCGCCGCAAGGCCAAGATCATCCGCGAC
TACGGCAAGCAGATGGCCGGCGACGACTGCGTGGCCGGCCGCCAGGACGAGGACTAA

Fig. 117

A

74. 2003_CON_H pol.PEP

FFRENLAFQQREARKFSPEQARANSPTSRELRVRRGDDPLSEAGAEGQGTSLSFPQITLWQRPLVTVKIEGQLREALLDTGA
DDTVLEEINLPGKWKPKMIGGIGGFIKVRQYEQVAIEICGKKAIGTVLVGPTPVNIIGRNILTQIGCTLNFPISPIETVPVK
LKPGMDGPKVKQWPLTEEKIKALTEICIEMEKEGKISKIGPENPYNTPIFAIKKKDSTKWRKLVDFRELNKRTQDFWEVQLG
IPHPAGLKKKKSVSVLDVGDAYFSVPLDKDFRKYTAFTIPSINNETPGIRYQYNVLPQGWKGSPAIFQSSMTKILEPFRKQN

PEMIIYQYMDDLYVGSDLEIGQHRAKIEELRAHLLRWGFTTPDKKHQKEPPFLWMGYELHPDKWTVQPVKLPEKDSWTVNDI
QKLVGKLNWASQIYPGIKVKQLCKLLRGAKALTDIVPLTKEAELELAENREILREPVHGVYYDPSKDLIAEIQKQGPDQWTY
QIYQEPFKNLKTGKYAKMRTAHTNDVKQLTEAVQKIATESIVIWGKIPKFRLPIQKETWETWWTEHWQATWIPEWEFVNTPH
LVKLWYQLETEPIAGAETYYVDGAANRETKIGKAGYVTDRGKQKVVSLTETTNQKTELQAIYLALQDSGLEVNIVTDSQYAL
GIIQAQPDKSESELVNQIIEELIKKEKVYLSWVPAHKGIGGNEQVDKLVSSGIRKVLFLDGIDKAQEEHERYHNNWRAMASD
FNLPPIVAKEIVASCDKCQLKGEAMHGQVDCSPGIWQLDCTHLEGKVILVAVHVASGYIEAEVIPAETGQETAYFILKLAGR
WPVKMIHTDNGSNFTSAAVKAACWWADIQQEFGIPYNPQSQGVVESMNKELKKIIGQVRDQAEHLRTAVQMAVFIHNFKRKG
GIGGYSAGERIIDIIATDIQTKELQKQISKIQKFRVYYRDSRDPIWKGPAKLLWKGEGAVVIQDNSEIKVVPRRKAKIIRDY
GKQMAGDDCVAGRQDED$

2003_CON_H pol.OPT

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TTCTTCCGCGAGAACCTGGCCTTCCAGCAGCGCGAGGCCCGCAAGTTCTCCCCCGAGCAGGCCCGCGCCAACTCCCCCACCT
CCCGCGAGCTGCGCGTGCGCCGCGGCGACGACCCCCTGTCCGAGGCCGGCGCCGAGGGCCAGGGCACCTCCCTGTCCTTCCC
CCAGATCACCCTGTGGCAGCGCCCCCTGGTGACCGTGAAGATCGAGGGCCAGCTGCGCGAGGCCCTGCTGGACACCGGCGCC
GACGACACCGTGCTGGAGGAGATCAACCTGCCCGGCAAGTGGAAGCCCAAGATGATCGGCGGCATCGGCGGCTTCATCAAGG
TGCGCCAGTACGAGCAGGTGGCCATCGAGATCTGCGGCAAGAAGGCCATCGGCACCGTGCTGGTGGGCCCCACCCCCGTGAA
CATCATCGGCCGCAACATCCTGACCCAGATCGGCTGCACCCTGAACTTCCCCATCTCCCCCATCGAGACCGTGCCCGTGAAG
CTGAAGCCCGGCATGGACGGCCCCAAGGTGAAGCAGTGGCCCCTGACCGAGGAGAAGATCAAGGCCCTGACCGAGATCTGCA
TCGAGATGGAGAAGGAGGGCAAGATCTCCAAGATCGGCCCCGAGAACCCCTACAACACCCCCATCTTCGCCATCAAGAAGAA
GGACTCCACCAAGTGGCGCAAGCTGGTGGACTTCCGCGAGCTGAACAAGCGCACCCAGGACTTCTGGGAGGTGCAGCTGGGC
ATCCCCCACCCCGCCGGCCTGAAGAAGAAGAAGTCCGTGTCCGTGCTGGACGTGGGCGACGCCTACTTCTCCGTGCCCCTGG
ACAAGGACTTCCGCAAGTACACCGCCTTCACCATCCCCTCCATCAACAACGAGACCCCCGGCATCCGCTACCAGTACAACGT
GCTGCCCCAGGGCTGGAAGGGCTCCCCCGCCATCTTCCAGTCCTCCATGACCAAGATCCTGGAGCCCTTCCGCAAGCAGAAC
CCCGAGATGATCATCTACCAGTACATGGACGACCTGTACGTGGGCTCCGACCTGGAGATCGGCCAGCACCGCGCCAAGATCG
AGGAGCTGCGCGCCCACCTGCTGCGCTGGGGCTTCACCACCCCCGACAAGAAGCACCAGAAGGAGCCCCCCTTCCTGTGGAT
GGGCTACGAGCTGCACCCCGACAAGTGGACCGTGCAGCCCGTGAAGCTGCCCGAGAAGGACTCCTGGACCGTGAACGACATC
CAGAAGCTGGTGGGCAAGCTGAACTGGGCCTCCCAGATCTACCCCGGCATCAAGGTGAAGCAGCTGTGCAAGCTGCTGCGCG
GCGCCAAGGCCCTGACCGACATCGTGCCCCTGACCAAGGAGGCCGAGCTGGAGCTGGCCGAGAACCGCGAGATCCTGCGCGA
GCCCGTGCACGGCGTGTACTACGACCCCTCCAAGGACCTGATCGCCGAGATCCAGAAGCAGGGCCCCGACCAGTGGACCTAC
CAGATCTACCAGGAGCCCTTCAAGAACCTGAAGACCGGCAAGTACGCCAAGATGCGCACCGCCCACACCAACGACGTGAAGC
AGCTGACCGAGGCCGTGCAGAAGATCGCCACCGAGTCCATCGTGATCTGGGGCAAGATCCCCAAGTTCCGCCTGCCCATCCA
GAAGGAGACCTGGGAGACCTGGTGGACCGAGCACTGGCAGGCCACCTGGATCCCCGAGTGGGAGTTCGTGAACACCCCCCAC
CTGGTGAAGCTGTGGTACCAGCTGGAGACCGAGCCCATCGCCGGCGCCGAGACCTACTACGTGGACGGCGCCGCCAACCGCG
AGACCAAGATCGGCAAGGCCGGCTACGTGACCGACCGCGGCAAGCAGAAGGTGGTGTCCCTGACCGAGACCACCAACCAGAA
GACCGAGCTGCAGGCCATCTACCTGGCCCTGCAGGACTCCGGCCTGGAGGTGAACATCGTGACCGACTCCCAGTACGCCCTG
GGCATCATCCAGGCCCAGCCCGACAAGTCCGAGTCCGAGCTGGTGAACCAGATCATCGAGGAGCTGATCAAGAAGGAGAAGG
TGTACCTGTCCTGGGTGCCCGCCCACAAGGGCATCGGCGGCAACGAGCAGGTGGACAAGCTGGTGTCCTCCGGCATCCGCAA
GGTGCTGTTCCTGGACGGCATCGACAAGGCCCAGGAGGAGCACGAGCGCTACCACAACAACTGGCGCGCCATGGCCTCCGAC
TTCAACCTGCCCCCCATCGTGGCCAAGGAGATCGTGGCCTCCTGCGACAAGTGCCAGCTGAAGGGCGAGGCCATGCACGGCC
AGGTGGACTGCTCCCCCGGCATCTGGCAGCTGGACTGCACCCACCTGGAGGGCAAGGTGATCCTGGTGGCCGTGCACGTGGC
CTCCGGCTACATCGAGGCCGAGGTGATCCCCGCCGAGACCGGCCAGGAGACCGCCTACTTCATCCTGAAGCTGGCCGGCCGC
TGGCCCGTGAAGATGATCCACACCGACAACGGCTCCAACTTCACCTCCGCCGCCGTGAAGGCCGCCTGCTGGTGGGCCGACA
TCCAGCAGGAGTTCGGCATCCCCTACAACCCCCAGTCCCAGGGCGTGGTGGAGTCCATGAACAAGGAGCTGAAGAAGATCAT
CGGCCAGGTGCGCGACCAGGCCGAGCACCTGCGCACCGCCGTGCAGATGGCCGTGTTCATCCACAACTTCAAGCGCAAGGGC
GGCATCGGCGGCTACTCCGCCGGCGAGCGCATCATCGACATCATCGCCACCGACATCCAGACCAAGGAGCTGCAGAAGCAGA
TCTCCAAGATCCAGAAGTTCCGCGTGTACTACCGCGACTCCCGCGACCCCATCTGGAAGGGCCCCGCCAAGCTGCTGTGGAA
GGGCGAGGGCGCCGTGGTGATCCAGGACAACTCCGAGATCAAGGTGGTGCCCCGCCGCAAGGCCAAGATCATCCGCGACTAC
GGCAAGCAGATGGCCGGCGACGACTGCGTGGCCGGCCGCCAGGACGAGGACTAA

Fig. 118 A

75. 2003_CON_01_AE pol.PEP

FFRENLAFQQGKAGEFSSEQTRANSPTSRKLGDGGRDNLLTEAGAERQGTSSSFSFPQITLWQRPLVTVKIGGQLKEALLDT
GADDTVLEDINLPGKWKPKMIGGIGGFIKVRQYDQILIEICGKKAIGTVLVGPTPVNIIGRNMLTQIGCTLNFPISPIDTVP
VTLKPGMDGPKVKQWPLTEEKIKALTEICKEMEEEGKISKIGPENPYNTPVFAIKKKDSTKWRKLVDFRELNKRTQDFWEVQ
LGIPHPAGLKKKKSVTVLDVGDAYFSVPLDESFRKYTAFTIPSINNETPGIRYQYNVLPQGWKGSPAIFQSSMTKILEPFRI
KNPEMVIYQYMDDLYVGSDLEIGQHRTKIEELRAHLLSWGFTTPDKKHQKEPPFLWMGYELHPDRWTVQPIELPEKDSWTVN
DIQKLVGKLNWASQIYAGIKVKQLCKLLRGAKALTDIVPLTEEAELELAENREILKTPVHGVYYDPSKDLVAEVQKQGQDQW
TYQIYQEPFKNLKTGKYARKRSAHTNDVRQLTEVVQKIATESIVIWGKTPKFRLPIQRETWETWWMEYWQATWIPEWEFVNT
PPLVKLWYQLEKDPIVGAETFYVDGAASRETKLGKAGYVTDRGRQKVVSLTETTNQKTELHAIHLALQDSGSEVNIVTDSQY
ALGIIQAQPDRSESEVVNQIIEELIKKEKVYLSWVPAHKGIGGNEQVDKLVSSGIRKVLFLDGIDKAQEEHERYHSNWRTMA

SDFNLPPIVAKEIVANCDKCQLKGEAMHGQVDCSPGIWQLDCTHLEGKVILVAVHVASGYIEAEVIPAETGQETAYFLLKLA
GRWPVKVIHTDNGSNFTSAAVKAACWWANVRQEFGIPYNPQSQGVVESMNKELKKIIGQVREQAEHLKTAVQMAVFIHNFKR
KGGIGGYSAGERIIDIIATDIQTKELQKQITKIQNFRVYYRDSRDPIWKGPAKLLWKGEGAVVIQDNSDIKVVPRRKAKIIR
DYGKQMAGDDCVAGRQDED$

2003_CON_01_AE pol.OPT

B

TTCTTCCGCGAGAACCTGGCCTTCCAGCAGGGCAAGGCCGGCGAGTTCTCCTCCGAGCAGACCCGCGCCAACTCCCCCACCT
CCCGCAAGCTGGGCGACGGCGGCCGCGACAACCTGCTGACCGAGGCCGGCGCCGAGCGCCAGGGCACCTCCTCCTCCTTCTC
CTTCCCCCAGATCACCCTGTGGCAGCGCCCCCTGGTGACCGTGAAGATCGGCGGCCAGCTGAAGGAGGCCCTGCTGGACACC
GGCGCCGACGACACCGTGCTGGAGGACATCAACCTGCCCGGCAAGTGGAAGCCCAAGATGATCGGCGGCATCGGCGGCTTCA
TCAAGGTGCGCCAGTACGACCAGATCCTGATCGAGATCTGCGGCAAGAAGGCCATCGGCACCGTGCTGGTGGGCCCCACCCC
CGTGAACATCATCGGCCGCAACATGCTGACCCAGATCGGCTGCACCCTGAACTTCCCCATCTCCCCCATCGACACCGTGCCC
GTGACCCTGAAGCCCGGCATGGACGGCCCCAAGGTGAAGCAGTGGCCCCTGACCGAGGAGAAGATCAAGGCCCTGACCGAGA
TCTGCAAGGAGATGGAGGAGGAGGGCAAGATCTCCAAGATCGGCCCCGAGAACCCCTACAACACCCCCGTGTTCGCCATCAA
GAAGAAGGACTCCACCAAGTGGCGCAAGCTGGTGGACTTCCGCGAGCTGAACAAGCGCACCCAGGACTTCTGGGAGGTGCAG
CTGGGCATCCCCCACCCCGCCGGCCTGAAGAAGAAGAAGTCCGTGACCGTGCTGGACGTGGGCGACGCCTACTTCTCCGTGC
CCCTGGACGAGTCCTTCCGCAAGTACACCGCCTTCACCATCCCCTCCATCAACAACGAGACCCCCGGCATCCGCTACCAGTA
CAACGTGCTGCCCCAGGGCTGGAAGGGCTCCCCCGCCATCTTCCAGTCCTCCATGACCAAGATCCTGGAGCCCTTCCGCATC
AAGAACCCCGAGATGGTGATCTACCAGTACATGGACGACCTGTACGTGGGCTCCGACCTGGAGATCGGCCAGCACCGCACCA
AGATCGAGGAGCTGCGCGCCCACCTGCTGTCCTGGGGCTTCACCACCCCCGACAAGAAGCACCAGAAGGAGCCCCCCTTCCT
GTGGATGGGCTACGAGCTGCACCCCGACCGCTGGACCGTGCAGCCCATCGAGCTGCCCGAGAAGGACTCCTGGACCGTGAAC
GACATCCAGAAGCTGGTGGGCAAGCTGAACTGGGCCTCCCAGATCTACGCCGGCATCAAGGTGAAGCAGCTGTGCAAGCTGC
TGCGCGGCGCCAAGGCCCTGACCGACATCGTGCCCCTGACCGAGGAGGCCGAGCTGGAGCTGGCCGAGAACCGCGAGATCCT
GAAGACCCCCGTGCACGGCGTGTACTACGACCCCTCCAAGGACCTGGTGGCCGAGGTGCAGAAGCAGGGCCAGGACCAGTGG
ACCTACCAGATCTACCAGGAGCCCTTCAAGAACCTGAAGACCGGCAAGTACGCCCGCAAGCGCTCCGCCCACACCAACGACG
TGCGCCAGCTGACCGAGGTGGTGCAGAAGATCGCCACCGAGTCCATCGTGATCTGGGGCAAGACCCCCAAGTTCCGCCTGCC
CATCCAGCGCGAGACCTGGGAGACCTGGTGGATGGAGTACTGGCAGGCCACCTGGATCCCCGAGTGGGAGTTCGTGAACACC
CCCCCCCTGGTGAAGCTGTGGTACCAGCTGGAGAAGGACCCCATCGTGGGCGCCGAGACCTTCTACGTGGACGGCGCCGCCT
CCCGCGAGACCAAGCTGGGCAAGGCCGGCTACGTGACCGACCGCGGCCGCCAGAAGGTGGTGTCCCTGACCGAGACCACCAA
CCAGAAGACCGAGCTGCACGCCATCCACCTGGCCCTGCAGGACTCCGGCTCCGAGGTGAACATCGTGACCGACTCCCAGTAC
GCCCTGGGCATCATCCAGGCCCAGCCCGACCGCTCCGAGTCCGAGGTGGTGAACCAGATCATCGAGGAGCTGATCAAGAAGG
AGAAGGTGTACCTGTCCTGGGTGCCCGCCCACAAGGGCATCGGCGGCAACGAGCAGGTGGACAAGCTGGTGTCCTCCGGCAT
CCGCAAGGTGCTGTTCCTGGACGGCATCGACAAGGCCCAGGAGGAGCACGAGCGCTACCACTCCAACTGGCGCACCATGGCC
TCCGACTTCAACCTGCCCCCCATCGTGGCCAAGGAGATCGTGGCCAACTGCGACAAGTGCCAGCTGAAGGGCGAGGCCATGC
ACGGCCAGGTGGACTGCTCCCCCGGCATCTGGCAGCTGGACTGCACCCACCTGGAGGGCAAGGTGATCCTGGTGGCCGTGCA
CGTGGCCTCCGGCTACATCGAGGCCGAGGTGATCCCCGCCGAGACCGGCCAGGAGACCGCCTACTTCCTGCTGAAGCTGGCC
GGCCGCTGGCCCGTGAAGGTGATCCACACCGACAACGGCTCCAACTTCACCTCCGCCGCCGTGAAGGCCGCCTGCTGGTGGG
CCAACGTGCGCCAGGAGTTCGGCATCCCCTACAACCCCCAGTCCCAGGGCGTGGTGGAGTCCATGAACAAGGAGCTGAAGAA
GATCATCGGCCAGGTGCGCGAGCAGGCCGAGCACCTGAAGACCGCCGTGCAGATGGCCGTGTTCATCCACAACTTCAAGCGC
AAGGGCGGCATCGGCGGCTACTCCGCCGGCGAGCGCATCATCGACATCATCGCCACCGACATCCAGACCAAGGAGCTGCAGA
AGCAGATCACCAAGATCCAGAACTTCCGCGTGTACTACCGCGACTCCCGCGACCCCATCTGGAAGGGCCCCGCCAAGCTGCT
GTGGAAGGGCGAGGGCGCCGTGGTGATCCAGGACAACTCCGACATCAAGGTGGTGCCCCGCCGCAAGGCCAAGATCATCCGC
GACTACGGCAAGCAGATGGCCGGCGACGACTGCGTGGCCGGCCGCCAGGACGAGGACTAA

Fig. 119

76. 2003_CON_02_AG pol.PEP

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FFRENLAFQQGEARKFSSEQTGTNSPTSRELWDGGRDNLLSEAGTEGQGTISSFNFPQITLWQRPLVTVRIGGQLIEALLDT
GADDTVLEEINLPGKWKPKMIGGIGGFIKVRQYDQILIEICGKKAIGTVLVGPTPVNIIGRNMLTQIGCTLNFPISPIETVP
VKLKPGMDGPKVKQWPLTEEKIKALTDICTEMEKEGKISKIGPENPYNTPVFAIKKKDSTKWRKLVDFRELNKRTQDFWEVQ
LGIPHPAGLKKKKSVTVLDVGDAYFSVPLDKDFRKYTAFTIPSVNNETPGIRYQYNVLPQGWKGSPAIFQASMTKILEPFRT
KNPEIVIYQYMDDLYVGSDLEIGQHRAKIEELREHLLRWGFTTPDKKHQKEPPFLWMGYELHPDKWTVQPIQLPEKDSWTVN
DIQKLVGKLNWASQIYAGIKVKQLCKLLRGAKALTDIVTLTEEAELELAENREILKEPVHGVYYDPTKDLIAEIQKQGQDQW
TYQIYQEPFKNLKTGKYAKMRSAHTNDVKQLTEVVQKVATESIVIWGKTPKFRLPIQRETWEAWWMEYWQATWIPEWEFVNT
PPLVKLWYQLEKDPIVGAETFYVDGAANRETKLGKAGYVTDRGRQKVVSLTETTNQKTELHAIHLALQDSGSEVNIVTDSQY
ALGIIQAQPDRSESELVNQIIEKLIEKDKVYLSWVPAHKGIGGNEQVDKLVSNGIRKVLFLDGIDKAQEEHERYHSNWRAMA
SDFNLPPIVAKEIVASCDKCQLKGEAMHGQVDCSPGIWQLDCTHLEGKIILVAVHVASGYIEAEVIPAETGQETAYFILKLA
GRWPVKVIHTDNGSNFTSAAVKAACWWANVTQEFGIPYNPQSQGVVESMNKELKKIIGQVRDQAEHLKTAVQMAVFIHNFKR
KGGIGGYSAGERIIDIIASDIQTKELQKQITKIQNFRVYYRDSRDPIWKGPAKLLWKGEGAVVIQDNSDIKVVPRRKAKIIR
DYGKQMAGDDCVAGRQDED$

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2003_CON_02_AG pol.OPT

TTCTTCCGCGAGAACCTGGCCTTCCAGCAGGGCGAGGCCCGCAAGTTCTCCTCCGAGCAGACCGGCACCAACTCCCCCACCT
CCCGCGAGCTGTGGGACGGCGGCCGCGACAACCTGCTGTCCGAGGCCGGCACCGAGGGCCAGGGCACCATCTCCTCCTTCAA
CTTCCCCCAGATCACCCTGTGGCAGCGCCCCCTGGTGACCGTGCGCATCGGCGGCCAGCTGATCGAGGCCCTGCTGGACACC
GGCGCCGACGACACCGTGCTGGAGGAGATCAACCTGCCCGGCAAGTGGAAGCCCAAGATGATCGGCGGCATCGGCGGCTTCA
TCAAGGTGCGCCAGTACGACCAGATCCTGATCGAGATCTGCGGCAAGAAGGCCATCGGCACCGTGCTGGTGGGCCCCACCCC
CGTGAACATCATCGGCCGCAACATGCTGACCCAGATCGGCTGCACCCTGAACTTCCCCATCTCCCCCATCGAGACCGTGCCC
GTGAAGCTGAAGCCCGGCATGGACGGCCCCAAGGTGAAGCAGTGGCCCCTGACCGAGGAGAAGATCAAGGCCCTGACCGACA
TCTGCACCGAGATGGAGAAGGAGGGCAAGATCTCCAAGATCGGCCCCGAGAACCCCTACAACACCCCCGTGTTCGCCATCAA
GAAGAAGGACTCCACCAAGTGGCGCAAGCTGGTGGACTTCCGCGAGCTGAACAAGCGCACCCAGGACTTCTGGGAGGTGCAG
CTGGGCATCCCCCACCCCGCCGGCCTGAAGAAGAAGAAGTCCGTGACCGTGCTGGACGTGGGCGACGCCTACTTCTCCGTGC
CCCTGGACAAGGACTTCCGCAAGTACACCGCCTTCACCATCCCCTCCGTGAACAACGAGACCCCCGGCATCCGCTACCAGTA
CAACGTGCTGCCCCAGGGCTGGAAGGGCTCCCCCCGCCATCTTCCAGGCCTCCATGACCAAGATCCTGGAGCCCTTCCGCACC
AAGAACCCCGAGATCGTGATCTACCAGTACATGGACGACCTGTACGTGGGCTCCGACCTGGAGATCGGCCAGCACCGCGCCA
AGATCGAGGAGCTGCGCGAGCACCTGCTGCGCTGGGGCTTCACCACCCCCGACAAGAAGCACCAGAAGGAGCCCCCCTTCCT
GTGGATGGGCTACGAGCTGCACCCCGACAAGTGGACCGTGCAGCCCATCCAGCTGCCCGAGAAGGACTCCTGGACCGTGAAC
GACATCCAGAAGCTGGTGGGCAAGCTGAACTGGGCCTCCCAGATCTACGCCGGCATCAAGGTGAAGCAGCTGTGCAAGCTGC
TGCGCGGCGCCAAGGCCCTGACCGACATCGTGACCCTGACCGAGGAGGCCGAGCTGGAGCTGGCCGAGAACCGCGAGATCCT
GAAGGAGCCCGTGCACGGCGTGTACTACGACCCCACCAAGGACCTGATCGCCGAGATCCAGAAGCAGGGCCAGGACCAGTGG
ACCTACCAGATCTACCAGGAGCCCTTCAAGAACCTGAAGACCGGCAAGTACGCCAAGATGCGCTCCGCCCACACCAACGACG
TGAAGCAGCTGACCGAGGTGGTGCAGAAGGTGGCCACCGAGTCCATCGTGATCTGGGGCAAGACCCCCAAGTTCCGCCTGCC
CATCCAGCGCGAGACCTGGGAGGCCTGGTGGATGGAGTACTGGCAGGCCACCTGGATCCCCGAGTGGGAGTTCGTGAACACC
CCCCCCCTGGTGAAGCTGTGGTACCAGCTGGAGAAGGACCCCATCGTGGGCGCCGAGACCTTCTACGTGGACGGCGCCGCCA
ACCGCGAGACCAAGCTGGGCAAGGCCGGCTACGTGACCGACCGCGGCCGCCAGAAGGTGGTGTCCCTGACCGAGACCACCAA
CCAGAAGACCGAGCTGCACGCCATCCACCTGGCCCTGCAGGACTCCGGCTCCGAGGTGAACATCGTGACCGACTCCCAGTAC
GCCCTGGGCATCATCCAGGCCCAGCCCGACCGCTCCGAGTCCGAGCTGGTGAACCAGATCATCGAGAAGCTGATCGAGAAGG
ACAAGGTGTACCTGTCCTGGGTGCCCGCCCACAAGGGCATCGGCGGCAACGAGCAGGTGGACAAGCTGGTGTCCAACGGCAT
CCGCAAGGTGCTGTTCCTGGACGGCATCGACAAGGCCCAGGAGGAGCACGAGCGCTACCACTCCAACTGGCGCGCCATGGCC
TCCGACTTCAACCTGCCCCCCATCGTGGCCAAGGAGATCGTGGCCTCCTGCGACAAGTGCCAGCTGAAGGGCGAGGCCATGC
ACGGCCAGGTGGACTGCTCCCCCGGCATCTGGCAGCTGGACTGCACCCACCTGGAGGGCAAGATCATCCTGGTGGCCGTGCA
CGTGGCCTCCGGCTACATCGAGGCCGAGGTGATCCCCGCCGAGACCGGCCAGGAGACCGCCTACTTCATCCTGAAGCTGGCC
GGCCGCTGGCCCGTGAAGGTGATCCACACCGACAACGGCTCCAACTTCACCTCCGCCGCCGTGAAGGCCGCCTGCTGGTGGG
CCAACGTGACCCAGGAGTTCGGCATCCCCTACAACCCCCAGTCCCAGGGCGTGGTGGAGTCCATGAACAAGGAGCTGAAGAA
GATCATCGGCCAGGTGCGCGACCAGGCCGAGCACCTGAAGACCGCCGTGCAGATGGCCGTGTTCATCCACAACTTCAAGCGC
AAGGGCGGCATCGGCGGCTACTCCGCCGGCGAGCGCATCATCGACATCATCGCCTCCGACATCCAGACCAAGGAGCTGCAGA
AGCAGATCACCAAGATCCAGAACTTCCGCGTGTACTACCGCGACTCCCGCGACCCCATCTGGAAGGGCCCCGCCAAGCTGCT
GTGGAAGGGCGAGGGCGCCGTGGTGATCCAGGACAACTCCGACATCAAGGTGGTGCCCCGCCGCAAGGCCAAGATCATCCGC
GACTACGGCAAGCAGATGGCCGGCGACGACTGCGTGGCCGGCCGCCAGGACGAGGACTAA

Fig. 120

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77. 2003_CON_03_AB pol.PEP

FFRENLAFQQREARKFSSEQTRAISPTSRKLWDGGRDNPLPETGTERQGTASSFNFPQITLWQRPLVTVRIGGQLKEALLDT
GADDTVLEDINLPGKWKPKMIGGIGGFIKVRQYDQILIEICGKKAIGTVLVGPTPVNIIGRNMLTQLGCTLNFPISPIETVP
VTLKPGMDGPKVKQWPLTEEKIKALTDICKEMEKEGKISKIGPENPYNTPVFAIKKKDSTKWRKLVDFRELNKRTQDFWEVQ
LGIPHPAGLKKKKSVTVLDVGDAYFSVPLDQDFRKYTAFTIPSTNNETPGIRYQYNVLPQGWKGSPAIFQSSMTKILEPFRK
QNPEIVIYQYMDDLYVGSDLEIGQHRTKIEELREHLLRWGFTTPDKKHQKEPPFLWMGYELHPDKWTVQPIVLPEKDSWTVN
DIQKLVGKLNWASQIYAGIKVRQLCKLLRGAKALTEVIPLTAEAELELAENREILKEPVHGVYYDPSKDLVAEIQKQGQGQW
TYQIYQEPFKNLKTGKYARLRGAHTNDVKQLTEAVQKIATESIVIWGKTPKFKLPIQKETWETWWTEYWQATWIPEWEFVNT
PPLVKLWYQLEKEPIVGAETFYVDGAANRETKSGKAGYVTDRGRQKVVSLTDTTNQKTELQAIHLALQDSGLEVNIVTDSQY
ALGIIQAQPDKSESELVSQIIEQLIKKEKVYLAWVPAHKGIGGNEQVDKLVSAGIRKVLFLDGIDKAQEAHEKYHSNWRAMA
SDFNLPPVVAKEIVASCDKCQLKGEAMHGQVDCSPGIWQLDCTHLEGKIILVAVHVASGYIEAEVIPAETGQETAYFVLKLA
GRWPVKIIHTDNGSNFISTAVKAACWWAGIKQEFGIPYNPQSQGVVESMNKQLKQIIGQVRDQAEHLKTAVQMAVFIHNFKR
KGGIGGYSAGERIIDIIATDIQTKELQKQIIKIQNFRVYYRDSRDPIWKGPAKLLWKGEGAVVIQDNNDIKVVPRRKAKIIR
DYGKQMAGDDCVASRQDED$

2003_CON_03_AB pol.OPT

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TTCTTCCGCGAGAACCTGGCCTTCCAGCAGCGCGAGGCCCGCAAGTTCTCCTCCGAGCAGACCCGCGCCATCTCCCCCACCT
CCCGCAAGCTGTGGGACGGCGGCCGCGACAACCCCCTGCCCGAGACCGGCACCGAGCGCCAGGGCACCGCCTCCTCCTTCAA
CTTCCCCCAGATCACCCTGTGGCAGCGCCCCCTGGTGACCGTGCGCATCGGCGGCCAGCTGAAGGAGGCCCTGCTGGACACC
GGCGCCGACGACACCGTGCTGGAGGACATCAACCTGCCCGGCAAGTGGAAGCCCAAGATGATCGGCGGCATCGGCGGCTTCA

TCAAGGTGCGCCAGTACGACCAGATCCTGATCGAGATCTGCGGCAAGAAGGCCATCGGCACCGTGCTGGTGGGCCCCACCCC
CGTGAACATCATCGGCCGCAACATGCTGACCCAGCTGGGCTGCACCCTGAACTTCCCCATCTCCCCCATCGAGACCGTGCCC
GTGACCCTGAAGCCCGGCATGGACGGCCCCAAGGTGAAGCAGTGGCCCCTGACCGAGGAGAAGATCAAGGCCCTGACCGACA
TCTGCAAGGAGATGGAGAAGGAGGGCAAGATCTCCAAGATCGGCCCCGAGAACCCCTACAACACCCCCGTGTTCGCCATCAA
GAAGAAGGACTCCACCAAGTGGCGCAAGCTGGTGGACTTCCGCGAGCTGAACAAGCGCACCCAGGACTTCTGGGAGGTGCAG
CTGGGCATCCCCCACCCCGCCGGCCTGAAGAAGAAGAAGTCCGTGACCGTGCTGGACGTGGGCGACGCCTACTTCTCCGTGC
CCCTGGACCAGGACTTCCGCAAGTACACCGCCTTCACCATCCCCTCCACCAACAACGAGACCCCCGGCATCCGCTACCAGTA
CAACGTGCTGCCCCAGGGCTGGAAGGGCTCCCCCGCCATCTTCCAGTCCTCCATGACCAAGATCCTGGAGCCCTTCCGCAAG
CAGAACCCCGAGATCGTGATCTACCAGTACATGGACGACCTGTACGTGGGCTCCGACCTGGAGATCGGCCAGCACCGCACCA
AGATCGAGGAGCTGCGCGAGCACCTGCTGCGCTGGGGCTTCACCACCCCCGACAAGAAGCACCAGAAGGAGCCCCCCTTCCT
GTGGATGGGCTACGAGCTGCACCCCGACAAGTGGACCGTGCAGCCCATCGTGCTGCCCGAGAAGGACTCCTGGACCGTGAAC
GACATCCAGAAGCTGGTGGGCAAGCTGAACTGGGCCTCCCAGATCTACGCCGGCATCAAGGTGCGCCAGCTGTGCAAGCTGC
TGCGCGGCGCCAAGGCCCTGACCGAGGTGATCCCCCTGACCGCCGAGGCCGAGCTGGAGCTGGCCGAGAACCGCGAGATCCT
GAAGGAGCCCGTGCACGGCGTGTACTACGACCCCTCCAAGGACCTGGTGGCCGAGATCCAGAAGCAGGGCCAGGGCCAGTGG
ACCTACCAGATCTACCAGGAGCCCTTCAAGAACCTGAAGACCGGCAAGTACGCCCGCCTGCGCGGCGCCCACACCAACGACG
TGAAGCAGCTGACCGAGGCCGTGCAGAAGATCGCCACCGAGTCCATCGTGATCTGGGGCAAGACCCCCAAGTTCAAGCTGCC
CATCCAGAAGGAGACCTGGGAGACCTGGTGGACCGAGTACTGGCAGGCCACCTGGATCCCCGAGTGGGAGTTCGTGAACACC
CCCCCCCTGGTGAAGCTGTGGTACCAGCTGGAGAAGGAGCCCATCGTGGGCGCCGAGACCTTCTACGTGGACGGCGCCGCCA
ACCGCGAGACCAAGTCCGGCAAGGCCGGCTACGTGACCGACCGCGGCCGCCAGAAGGTGGTGTCCCTGACCGACACCACCAA
CCAGAAGACCGAGCTGCAGGCCATCCACCTGGCCCTGCAGGACTCCGGCCTGGAGGTGAACATCGTGACCGACTCCCAGTAC
GCCCTGGGCATCATCCAGGCCCAGCCCGACAAGTCCGAGTCCGAGCTGGTGTCCCAGATCATCGAGCAGCTGATCAAGAAGG
AGAAGGTGTACCTGGCCTGGGTGCCCGCCCACAAGGGCATCGGCGGCAACGAGCAGGTGGACAAGCTGGTGTCCGCCGGCAT
CCGCAAGGTGCTGTTCCTGGACGGCATCGACAAGGCCCAGGAGGCCCACGAGAAGTACCACTCCAACTGGCGCGCCATGGCC
TCCGACTTCAACCTGCCCCCCGTGGTGGCCAAGGAGATCGTGGCCTCCTGCGACAAGTGCCAGCTGAAGGGCGAGGCCATGC
ACGGCCAGGTGGACTGCTCCCCCGGCATCTGGCAGCTGGACTGCACCCACCTGGAGGGCAAGATCATCCTGGTGGCCGTGCA
CGTGGCCTCCGGCTACATCGAGGCCGAGGTGATCCCCGCCGAGACCGGCCAGGAGACCGCCTACTTCGTGCTGAAGCTGGCC
GGCCGCTGGCCCGTGAAGATCATCCACACCGACAACGGCTCCAACTTCATCTCCACCGCCGTGAAGGCCGCCTGCTGGTGGG
CCGGCATCAAGCAGGAGTTCGGCATCCCCTACAACCCCCAGTCCCAGGGCGTGGTGGAGTCCATGAACAAGCAGCTGAAGCA
GATCATCGGCCAGGTGCGCGACCAGGCCGAGCACCTGAAGACCGCCGTGCAGATGGCCGTGTTCATCCACAACTTCAAGCGC
AAGGGCGGCATCGGCGGCTACTCCGCCGGCGAGCGCATCATCGACATCATCGCCACCGACATCCAGACCAAGGAGCTGCAGA
AGCAGATCATCAAGATCCAGAACTTCCGCGTGTACTACCGCGACTCCCGCGACCCCATCTGGAAGGGCCCCGCCAAGCTGCT
GTGGAAGGGCGAGGGCGCCGTGGTGATCCAGGACAACAACGACATCAAGGTGGTGCCCCGCCGCAAGGCCAAGATCATCCGC
GACTACGGCAAGCAGATGGCCGGCGACGACTGCGTGGCCTCCCGCCAGGACGAGGACTAA

ig.12A

78. 2003_CON_04_CPX pol.PEP

FFRENVAFQQREARKFSSEQARANSPARRELRDERGDNLLSEAGTEGQGTISFNFPQITLWQRPLVTIKIGGQIREALLDTG
ADDTVLEEINLPGKWKPKMIGGIGGFIKVRQYDQIPIEICGKKAIGTVLVGPTPVNIIGRNMLTQLGCTLNFPISPIETVPV
KLKPGMDGPKVKQWPLTEEKIKALTEICTEMEKEGKISKIGPENPYNTPIFAIKKKNSTRWRKLVDFRELNKRTQDFWEVQL
GIPHPAGLKKKKSVTVLDVGDAYFSVPLDPEFRKYTAFTIPSTNNETPGIRYQYNVLPQGWKGSPAIFQCSMTKILEPFRTK
NPEIVIYQYMDDLYVGSDLEIGQHRAKIEELREHLLRWGFSTPDKKHQKEPPFLWMGYELHPDKWTVQPIQLAEKDSWTVND
IQKLVGKLNWASQIYPGIKVKQLCKLLRGAKALTDIVPLTTEAELELAENREILKEPVHGAYYDPSKDLIAEIQKQGQGQWT
YQIYQEPYKNLKTGKYAKTRSAHTNDVRQLTEAVQKIAMECIVIWGKTPKFRLPIQKETWDTWWTEYWQATWIPEWEFVNTP
PLVKLWYQLETDPIAGAETFYVDGAASRETKQGKAGYVTDRGRQKVVSLSETTNQKTELQAIYLALQDSGSEVNIVTDSQYA
IGIIQAQPDRSESDLVNQIIEQLIQKDKVYLSWVPAHKGIGGNEQVDKLVSNGIRKVLFLDGIDKAQEEHEKYHNNWRAMAS
DFNLPPVVAKEIVASCNKCQLKGEAMHGQVDCSPGIWQLDCTHLEGKIILVAVHVASGYIEAEVIPAETGQETAYFILKLAG
RWPVKIIHTDNGPNFTSAAVKAACWWADIQQEFGIPYNPQSQGVVESMNKELKKIIGQVRDQAEHLKTAVQMAVFIHNFKRK
GGIGGYSAGERIIDIIASDIQTKELQKQITKIQNFRVYYRDSRDPIWKGPAKLLWKGEGAVVIQDNSDIKVVPRRKAKIIRD
YGKQMAGDDCVAGRQDED$

2003_CON_04_CPX pol.OPT

TTCTTCCGCGAGAACGTGGCCTTCCAGCAGCGCGAGGCCCGCAAGTTCTCCTCCGAGCAGGCCCGCGCCAACTCCCCCGCCC
GCCGCGAGCTGCGCGACGAGCGCGGCGACAACCTGCTGTCCGAGGCCGGCACCGAGGGCCAGGGCACCATCTCCTTCAACTT
CCCCCAGATCACCCTGTGGCAGCGCCCCCTGGTGACCATCAAGATCGGCGGCCAGATCCGCGAGGCCCTGCTGGACACCGGC
GCCGACGACACCGTGCTGGAGGAGATCAACCTGCCCGGCAAGTGGAAGCCCAAGATGATCGGCGGCATCGGCGGCTTCATCA
AGGTGCGCCAGTACGACCAGATCCCCATCGAGATCTGCGGCAAGAAGGCCATCGGCACCGTGCTGGTGGGCCCCACCCCGT
GAACATCATCGGCCGCAACATGCTGACCCAGCTGGGCTGCACCCTGAACTTCCCCATCTCCCCCATCGAGACCGTGCCCGTG
AAGCTGAAGCCCGGCATGGACGGCCCCAAGGTGAAGCAGTGGCCCCTGACCGAGGAGAAGATCAAGGCCCTGACCGAGATCT
GCACCGAGATGGAGAAGGAGGGCAAGATCTCCAAGATCGGCCCCGAGAACCCCTACAACACCCCCATCTTCGCCATCAAGAA
GAAGAACTCCACCCGCTGGCGCAAGCTGGTGGACTTCCGCGAGCTGAACAAGCGCACCCAGGACTTCTGGGAGGTGCAGCTG

GGCATCCCCCACCCCGCCGGCCTGAAGAAGAAGAAGTCCGTGACCGTGCTGGACGTGGGCGACGCCTACTTCTCCGTGCCCC
TGGACCCCGAGTTCCGCAAGTACACCGCCTTCACCATCCCCTCCACCAACAACGAGACCCCCGGCATCCGCTACCAGTACAA
CGTGCTGCCCCAGGGCTGGAAGGGCTCCCCCGCCATCTTCCAGTGCTCCATGACCAAGATCCTGGAGCCCTTCCGCACCAAG
AACCCCGAGATCGTGATCTACCAGTACATGGACGACCTGTACGTGGGCTCCGACCTGGAGATCGGCCAGCACCGCGCCAAGA
TCGAGGAGCTGCGCGAGCACCTGCTGCGCTGGGGCTTCTCCACCCCCGACAAGAAGCACCAGAAGGAGCCCCCCTTCCTGTG
GATGGGCTACGAGCTGCACCCCGACAAGTGGACCGTGCAGCCCATCCAGCTGGCCGAGAAGGACTCCTGGACCGTGAACGAC
ATCCAGAAGCTGGTGGGCAAGCTGAACTGGGCCTCCCAGATCTACCCCGGCATCAAGGTGAAGCAGCTGTGCAAGCTGCTGC
GCGGCGCCAAGGCCCTGACCGACATCGTGCCCCTGACCACCGAGGCCGAGCTGGAGCTGGCCGAGAACCGCGAGATCCTGAA
GGAGCCCGTGCACGGCGCCTACTACGACCCCTCCAAGGACCTGATCGCCGAGATCCAGAAGCAGGGCCAGGGCCAGTGGACC
TACCAGATCTACCAGGAGCCCTACAAGAACCTGAAGACCGGCAAGTACGCCAAGACCCGCTCCGCCCACACCAACGACGTGC
GCCAGCTGACCGAGGCCGTGCAGAAGATCGCCATGGAGTGCATCGTGATCTGGGGCAAGACCCCCAAGTTCCGCCTGCCCAT
CCAGAAGGAGACCTGGGACACCTGGTGGACCGAGTACTGGCAGGCCACCTGGATCCCCGAGTGGGAGTTCGTGAACACCCCC
CCCCTGGTGAAGCTGTGGTACCAGCTGGAGACCGACCCCATCGCCGGCGCCGAGACCTTCTACGTGGACGGCGCCGCCTCCC
GCGAGACCAAGCAGGGCAAGGCCGGCTACGTGACCGACCGCGGCCGCCAGAAGGTGGTGTCCCTGTCCGAGACCACCAACCA
GAAGACCGAGCTGCAGGCCATCTACCTGGCCCTGCAGGACTCCGGCTCCGAGGTGAACATCGTGACCGACTCCCAGTACGCC
ATCGGCATCATCCAGGCCCAGCCCGACCGCTCCGAGTCCGACCTGGTGAACCAGATCATCGAGCAGCTGATCCAGAAGGACA
AGGTGTACCTGTCCTGGGTGCCCGCCCACAAGGGCATCGGCGGCAACGAGCAGGTGGACAAGCTGGTGTCCAACGGCATCCG
CAAGGTGCTGTTCCTGGACGGCATCGACAAGGCCCAGGAGGAGCACGAGAAGTACCACAACAACTGGCGCGCCATGGCCTCC
GACTTCAACCTGCCCCCCGTGGTGGCCAAGGAGATCGTGGCCTCCTGCAACAAGTGCCAGCTGAAGGGCGAGGCCATGCACG
GCCAGGTGGACTGCTCCCCCGGCATCTGGCAGCTGGACTGCACCCACCTGGAGGGCAAGATCATCCTGGTGGCCGTGCACGT
GGCCTCCGGCTACATCGAGGCCGAGGTGATCCCCGCCGAGACCGGCCAGGAGACCGCCTACTTCATCCTGAAGCTGGCCGGC
CGCTGGCCCGTGAAGATCATCCACACCGACAACGGCCCCAACTTCACCTCCGCCGCCGTGAAGGCCGCCTGCTGGTGGGCCG
ACATCCAGCAGGAGTTCGGCATCCCCTACAACCCCCAGTCCCAGGGCGTGGTGGAGTCCATGAACAAGGAGCTGAAGAAGAT
CATCGGCCAGGTGCGCGACCAGGCCGAGCACCTGAAGACCGCCGTGCAGATGGCCGTGTTCATCCACAACTTCAAGCGCAAG
GGCGGCATCGGCGGCTACTCCGCCGGCGAGCGCATCATCGACATCATCGCCTCCGACATCCAGACCAAGGAGCTGCAGAAGC
AGATCACCAAGATCCAGAACTTCCGCGTGTACTACCGCGACTCCCGCGACCCCATCTGGAAGGGCCCCGCCAAGCTGCTGTG
GAAGGGCGAGGGCGCCGTGGTGATCCAGGACAACTCCGACATCAAGGTGGTGCCCCGCCGCAAGGCCAAGATCATCCGCGAC
TACGGCAAGCAGATGGCCGGCGACGACTGCGTGGCCGGCCGCCAGGACGAGGACTAA

ig. 122

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79. 2003_CON_06_CPX pol.PEP

FFRENLAFQQGEAREFSSEQARANSPTRRELRVRRGDSPLPEAGAEGQGAISLSFPQITLWQRPLVTVRIGGQLIEALLDTG
ADDTVLEDINLPGKWKPKMIGGIGGFIKVRQYDQILIEICGKKAIGTVLVGPTPVNIIGRNMLTQIGCTLNFPISPIETVPV
KLKPGMDGPKVKQWPLTEEKIKALTEICTEMEKEGKISKIGPENPYNTPIFAIKKKDSTKWRKLVDFRELNKRTQDFWEVQL
GIPHPAGLKKKKSVTVLDVGDAYFSVPLDEDFRKYTAFTIPSINNETPGIRYQYNVLPQGWKGSPAIFQSSMIKILEPFRIK
NPEIVIYQYMDDLYVGSDLEIGQHRAKIEELREHLLKWGFTTPDKKHQKEPPFLWMGYELHPDKWTVQPIQLPDKDSWTVND
IQKLVGKLNWASQIYPGIKVKQLCKLLRGAKALTDIVPLTAEAELELAENREILKEPVHGVYYDPSKDLIAEIQKQGQGQWT
YQIYQEPHKNLKTGKYARIKSAHTNDVKQLTEAVQKIALESIVIWGKTPKFRLPIQKETWETWWTEYWQATWIPEWEFVNTP
PLVKLWYQLETEPIVGAETFYVDGAANRETKKGKAGYVTDRGRQKVVSLTETTNQKTELQAINLALQDSGSEVNIVTDSQYA
LGIIQAQPDKSESELVNQIIEQLIKKEKVYLSWVPAHKGIGGNEQVDKLVSTGIRKVLFLDGIDKAQEDHERYHSNWRAMAS
DFNLPPIVAKEIVASCDKCQLKGEAMHGQVDCSPGIWQLDCTHLEGKIILVAVHVASGYIEAEVIPAETGQETAYFILKLAG
RWPVKVIHTDNGSNFTSAAVKAACWWANITQEFGIPYNPQSQGVVESMNKELKKIIGQVRDQAEHLKTAVQMAVFIHNFKRK
GGIGGYSAGERIIDIIASDIQTKELQKQITKIQNFRVYYRDSRDPIWKGPAKLLWKGEGAVVIQDNSEIKVVPRRKAKIIRD
YGKQMAGDDCVAGRQDED$

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2003_CON_06_CPX pol.OPT

TTCTTCCGCGAGAACCTGGCCTTCCAGCAGGGCGAGGCCCGCGAGTTCTCCTCCGAGCAGGCCCGCGCCAACTCCCCCACCC
GCCGCGAGCTGCGCGTGCGCCGCGGCGACTCCCCCCTGCCCGAGGCCGGCGCCGAGGGCCAGGGCGCCATCTCCCTGTCCTT
CCCCCAGATCACCCTGTGGCAGCGCCCCCTGGTGACCGTGCGCATCGGCGGCCAGCTGATCGAGGCCCTGCTGGACACCGGC
GCCGACGACACCGTGCTGGAGGACATCAACCTGCCCGGCAAGTGGAAGCCCAAGATGATCGGCGGCATCGGCGGCTTCATCA
AGGTGCGCCAGTACGACCAGATCCTGATCGAGATCTGCGGCAAGAAGGCCATCGGCACCGTGCTGGTGGGCCCCACCCCCGT
GAACATCATCGGCCGCAACATGCTGACCCAGATCGGCTGCACCCTGAACTTCCCCATCTCCCCCATCGAGACCGTGCCCGTG
AAGCTGAAGCCCGGCATGGACGGCCCCAAGGTGAAGCAGTGGCCCCTGACCGAGGAGAAGATCAAGGCCCTGACCGAGATCT
GCACCGAGATGGAGAAGGAGGGCAAGATCTCCAAGATCGGCCCCGAGAACCCCTACAACACCCCCATCTTCGCCATCAAGAA
GAAGGACTCCACCAAGTGGCGCAAGCTGGTGGACTTCCGCGAGCTGAACAAGCGCACCCAGGACTTCTGGGAGGTGCAGCTG
GGCATCCCCCACCCCGCCGGCCTGAAGAAGAAGAAGTCCGTGACCGTGCTGGACGTGGGCGACGCCTACTTCTCCGTGCCCC
TGGACGAGGACTTCCGCAAGTACACCGCCTTCACCATCCCCTCCATCAACAACGAGACCCCCGGCATCCGCTACCAGTACAA
CGTGCTGCCCCAGGGCTGGAAGGGCTCCCCCGCCATCTTCCAGTCCTCCATGATCAAGATCCTGGAGCCCTTCCGCATCAAG
AACCCCGAGATCGTGATCTACCAGTACATGGACGACCTGTACGTGGGCTCCGACCTGGAGATCGGCCAGCACCGCGCCAAGA
TCGAGGAGCTGCGCGAGCACCTGCTGAAGTGGGGCTTCACCACCCCCGACAAGAAGCACCAGAAGGAGCCCCCCTTCCTGTG

GATGGGCTACGAGCTGCACCCCGACAAGTGGACCGTGCAGCCCATCCAGCTGCCCGACAAGGACTCCTGGACCGTGAACGAC
ATCCAGAAGCTGGTGGGCAAGCTGAACTGGGCCTCCCAGATCTACCCCGGCATCAAGGTGAAGCAGCTGTGCAAGCTGCTGC
GCGGCGCCAAGGCCCTGACCGACATCGTGCCCCTGACCGCCGAGGCCGAGCTGGAGCTGGCCGAGAACCGCGAGATCCTGAA
GGAGCCCGTGCACGGCGTGTACTACGACCCCTCCAAGGACCTGATCGCCGAGATCCAGAAGCAGGGCCAGGGCCAGTGGACC
TACCAGATCTACCAGGAGCCCCACAAGAACCTGAAGACCGGCAAGTACGCCCGCATCAAGTCCGCCCACACCAACGACGTGA
AGCAGCTGACCGAGGCCGTGCAGAAGATCGCCCTGGAGTCCATCGTGATCTGGGGCAAGACCCCCAAGTTCCGCCTGCCCAT
CCAGAAGGAGACCTGGGAGACCTGGTGGACCGAGTACTGGCAGGCCACCTGGATCCCCGAGTGGGAGTTCGTGAACACCCCC
CCCCTGGTGAAGCTGTGGTACCAGCTGGAGACCGAGCCCATCGTGGGCGCCGAGACCTTCTACGTGGACGGCGCCGCCAACC
GCGAGACCAAGAAGGGCAAGGCCGGCTACGTGACCGACCGCGGCCGCCAGAAGGTGGTGTCCCTGACCGAGACCACCAACCA
GAAGACCGAGCTGCAGGCCATCAACCTGGCCCTGCAGGACTCCGGCTCCGAGGTGAACATCGTGACCGACTCCCAGTACGCC
CTGGGCATCATCCAGGCCCAGCCCGACAAGTCCGAGTCCGAGCTGGTGAACCAGATCATCGAGCAGCTGATCAAGAAGGAGA
AGGTGTACCTGTCCTGGGTGCCCGCCCACAAGGGCATCGGCGGCAACGAGCAGGTGGACAAGCTGGTGTCCACCGGCATCCG
CAAGGTGCTGTTCCTGGACGGCATCGACAAGGCCCAGGAGGACCACGAGCGCTACCACTCCAACTGGCGCGCCATGGCCTCC
GACTTCAACCTGCCCCCCATCGTGGCCAAGGAGATCGTGGCCTCCTGCGACAAGTGCCAGCTGAAGGGCGAGGCCATGCACG
GCCAGGTGGACTGCTCCCCCGGCATCTGGCAGCTGGACTGCACCCACCTGGAGGGCAAGATCATCCTGGTGGCCGTGCACGT
GGCCTCCGGCTACATCGAGGCCGAGGTGATCCCCGCCGAGACCGGCCAGGAGACCGCCTACTTCATCCTGAAGCTGGCCGGC
CGCTGGCCCGTGAAGGTGATCCACACCGACAACGGCTCCAACTTCACCTCCGCCGCCGTGAAGGCCGCCTGCTGGTGGGCCA
ACATCACCCAGGAGTTCGGCATCCCCTACAACCCCCAGTCCCAGGGCGTGGTGGAGTCCATGAACAAGGAGCTGAAGAAGAT
CATCGGCCAGGTGCGCGACCAGGCCGAGCACCTGAAGACCGCCGTGCAGATGGCCGTGTTCATCCACAACTTCAAGCGCAAG
GGCGGCATCGGCGGCTACTCCGCCGGCGAGCGCATCATCGACATCATCGCCTCCGACATCCAGACCAAGGAGCTGCAGAAGC
AGATCACCAAGATCCAGAACTTCCGCGTGTACTACCGCGACTCCCGCGACCCCATCTGGAAGGGCCCCGCCAAGCTGCTGTG
GAAGGGCGAGGGCGCCGTGGTGATCCAGGACAACTCCGAGATCAAGGTGGTGCCCCGCCGCAAGGCCAAGATCATCCGCGAC
TACGGCAAGCAGATGGCCGGCGACGACTGCGTGGCCGGCCGCCAGGACGAGGACTAA

Fig. 123

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80. 2003_CON_08_BC pol.PEP

FFREILAFPQGEAREFPPEQTRANSPTSRELQVRGDNPSSEAGTERQGTLNFPQITLWQRPLVSIKVGGQIKEALLDTGADD
TVLEEVNLPGKWKPKMIGGIGGFIKVRQYEQIPIEICGKKAIGTVLVGPTPVNIIGRNMLTQLGCTLNFPISPIETVPVKLK
PGMDGPKVKQWPLTEEKIKALTAICDEMEKEGKITKIGPDNPYNTPIFAIRKKDSSKWRKLVDFRELNKRTQDFWEVQLGIP
HPAGLKKKKSVTVLDVGDAYFSVPLDKDFRKYTAFTIPSVNNETPGIRYQYNVLPQGWKGSPAIFQCSMTKILEPFRKQNPD
IVIYQYMDDLYVGSDLEIGQHRTKIEELREHLLKWGFTTPDKKHQKEPPFLWMGYELHPDKWTVQPIQLPEKDSWTVNDIQK
LVGKLNWASQIYPGIKVRQLCKLLRGAKALTDIVPLTEEAELELAENREILKEPVHGAYYDPSKELIAEIQKQGQDQWTYQI
YQEPFKNLKTGKYAKMRTAHTNDVKQLTEAVQKIAMESIVIWGKIPKFRLPIQKETWETWWTDYWQATWIPEWEFVNTPPLV
KLWYQLEKDPIAGVETFYVDGAANRETKIGKAGYVTDRGRKKIVSLTDTTNQKTELQAIYIALQDSGSEVNIVTDSQYALGI
IQAQPDKSESELVNQIIEQLIKKERVYLSWVPAHKGIGGNEQVDKLVSNGIRKVLFLDGIDKAQEEHEKYHSNWRAMASDFN
LPPIVAKEIVASCDQCQLKGEAMHGQVDCSPGIWQLDCTHLEGKIILVAVHVASGYIEAEVIPAETGQETAYFILKLAGRWP
VKVIHTDNGSNFTSAAVKAACWWAGIQQEFGIPYNPQSQGVVESMNKELKKLIGQVRDQAEHLKTAVQMAVFIHNFKRKGGI
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QMAGADCVAGRQDED$

2003_CON_08_BC pol.OPT

B

TTCTTCCGCGAGATCCTGGCCTTCCCCCAGGGCGAGGCCCGCGAGTTCCCCCCCGAGCAGACCCGCGCCAACTCCCCCACCT
CCCGCGAGCTGCAGGTGCGCGGCGACAACCCCTCCTCCGAGGCCGGCACCGAGCGCCAGGGCACCCTGAACTTCCCCCAGAT
CACCCTGTGGCAGCGCCCCCTGGTGTCCATCAAGGTGGGCGGCCAGATCAAGGAGGCCCTGCTGGACACCGGCGCCGACGAC
ACCGTGCTGGAGGAGGTGAACCTGCCCGGCAAGTGGAAGCCCAAGATGATCGGCGGCATCGGCGGCTTCATCAAGGTGCGCC
AGTACGAGCAGATCCCCATCGAGATCTGCGGCAAGAAGGCCATCGGCACCGTGCTGGTGGGCCCCACCCCCGTGAACATCAT
CGGCCGCAACATGCTGACCCAGCTGGGCTGCACCCTGAACTTCCCCATCTCCCCCATCGAGACCGTGCCCGTGAAGCTGAAG
CCCGGCATGGACGGCCCCAAGGTGAAGCAGTGGCCCCTGACCGAGGAGAAGATCAAGGCCCTGACCGCCATCTGCGACGAGA
TGGAGAAGGAGGGCAAGATCACCAAGATCGGCCCCGACAACCCCTACAACACCCCCATCTTCGCCATCCGCAAGAAGGACTC
CTCCAAGTGGCGCAAGCTGGTGGACTTCCGCGAGCTGAACAAGCGCACCCAGGACTTCTGGGAGGTGCAGCTGGGCATCCCC
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CTGGTGGGCAAGCTGAACTGGGCCTCCCAGATCTACCCCGGCATCAAGGTGCGCCAGCTGTGCAAGCTGCTGCGCGGCGCCA
AGGCCCTGACCGACATCGTGCCCCTGACCGAGGAGGCCGAGCTGGAGCTGGCCGAGAACCGCGAGATCCTGAAGGAGCCCGT
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TACCAGGAGCCCTTCAAGAACCTGAAGACCGGCAAGTACGCCAAGATGCGCACCGCCCACACCAACGACGTGAAGCAGCTGA

CCGAGGCCGTGCAGAAGATCGCCATGGAGTCCATCGTGATCTGGGGCAAGATCCCCAAGTTCCGCCTGCCCATCCAGAAGGA
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ATCCAGGCCCAGCCCGACAAGTCCGAGTCCGAGCTGGTGAACCAGATCATCGAGCAGCTGATCAAGAAGGAGCGCGTGTACC
TGTCCTGGGTGCCCGCCCACAAGGGCATCGGCGGCAACGAGCAGGTGGACAAGCTGGTGTCCAACGGCATCCGCAAGGTGCT
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ACTGCTCCCCCGGCATCTGGCAGCTGGACTGCACCCACCTGGAGGGCAAGATCATCCTGGTGGCCGTGCACGTGGCCTCCGG
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GGGCGCCGTGGTGATCCAGGACAACTCCGACATCAAGGTGGTGCCCCGCCGCAAGGCCAAGATCATCAAGGACTACGGCAAG
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9.124

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81. 2003_CON_10_CD pol.PEP

FFRENLAFQQRKARELPSEQTRANSPTSRELRVWGGDNTLSETGAERQGAVSLSFPQITLWQRPLVTVKIGGQLKEALLDTG
ADDTVLEEMNLPGKWKPKMIGGIGGFIKVRQYDQILIEICGYKAIGTVLVGPTPVNIIGRNLLTQIGCTLNFPISPIETVPV
KLKPGMDGPKVKQWPLTEEKIKALTEICTEMEKEGKISRIGPENPYNTPIFAIKKKDSTKWRKLVDFRELNKRTQDFWEVQL
GIPHPAGLKKKKSVTVLDVGDAYFSVPLYEDFRKYTAFTIPSINNETPGIRYQYNVLPQGWKGSPAIFQSSMTKILEPFRKQ
NPEMVIYQYMDDLYVGSDLEIGQHRIKIEELRGHLLKWGFTTPDKKHQKEPPFLWMGYELHPDKWTVQPIQLPEKDSWTVND
IQKLVGKLNWASQIYPGIKVRQLCKLLRGAKALTDIVPLTEEAELELAENREILKEPVHGVYYDPSKDLIAEIQKQGQDQWT
YQIYQEPHKNLKTGKYAKRRTAHTNDVKQLTEAVQKIAQESIVIWGKTPKFRLPIQKETWETWWTDYWQATWIPEWEFVNTP
PLVKLWYQLEKEPIVGAETFYVDGAANRETKLGKAGYVTDRGRQKVISITDTTNQKTELQAINLALQDSGSEVNIVTDSQYA
LGIIQAQPDKSESELVNQIIEQLIKKEKVYLSWVPAHKGIGGNEQVDKLVSSGIRKVLFLDGIDKAQEEHEKYHNNWRAMAS
DFNLPPVVAKEIVASCDKCQLKGEALHGQVDCSPGIWQLDCTHLEGKVILVAVHVASGYIEAEVIPAETGQETAYFLLKLAG
RWPVKVVHTDNGSNFTSAAVKAACWWAGIKQEFGIPYNPQSQGVVESMNKELKKIIGQVRDQAEHLKTAVQMAVFIHNFKRK
GGIGGYSAGERIIDIIATDIQTKELQKQIIKIQNFRVYYRDSRDPIWKGPAKLLWKGEGAVVIQDNSDIKVVPRRKVKIIKD
YGKQMAGADCVASRQDEDQ

2003_CON_10_CD pol.OPT

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TTCTTCCGCGAGAACCTGGCCTTCCAGCAGCGCAAGGCCCGCGAGCTGCCCTCCGAGCAGACCCGCGCCAACTCCCCCACCT
CCCGCGAGCTGCGCGTGTGGGGCGGCGACAACACCCTGTCCGAGACCGGCGCCGAGCGCCAGGGCGCCGTGTCCCTGTCCTT
CCCCCAGATCACCCTGTGGCAGCGCCCCCTGGTGACCGTGAAGATCGGCGGCCAGCTGAAGGAGGCCCTGCTGGACACCGGC
GCCGACGACACCGTGCTGGAGGAGATGAACCTGCCCGGCAAGTGGAAGCCCAAGATGATCGGCGGCATCGGCGGCTTCATCA
AGGTGCGCCAGTACGACCAGATCCTGATCGAGATCTGCGGCTACAAGGCCATCGGCACCGTGCTGGTGGGCCCCACCCCCGT
GAACATCATCGGCCGCAACCTGCTGACCCAGATCGGCTGCACCCTGAACTTCCCCATCTCCCCCATCGAGACCGTGCCCGTG
AAGCTGAAGCCCGGCATGGACGGCCCCAAGGTGAAGCAGTGGCCCCTGACCGAGGAGAAGATCAAGGCCCTGACCGAGATCT
GCACCGAGATGGAGAAGGAGGGCAAGATCTCCCGCATCGGCCCCGAGAACCCCTACAACACCCCCATCTTCGCCATCAAGAA
GAAGGACTCCACCAAGTGGCGCAAGCTGGTGGACTTCCGCGAGCTGAACAAGCGCACCCAGGACTTCTGGGAGGTGCAGCTG
GGCATCCCCCACCCCGCCGGCCTGAAGAAGAAGAAGTCCGTGACCGTGCTGGACGTGGGCGACGCCTACTTCTCCGTGCCCC
TGTACGAGGACTTCCGCAAGTACACCGCCTTCACCATCCCCTCCATCAACAACGAGACCCCCGGCATCCGCTACCAGTACAA
CGTGCTGCCCCAGGGCTGGAAGGGCTCCCCCGCCATCTTCCAGTCCTCCATGACCAAGATCCTGGAGCCCTTCCGCAAGCAG
AACCCCGAGATGGTGATCTACCAGTACATGGACGACCTGTACGTGGGCTCCGACCTGGAGATCGGCCAGCACCGCATCAAGA
TCGAGGAGCTGCGCGGCCACCTGCTGAAGTGGGGCTTCACCACCCCCGACAAGAAGCACCAGAAGGAGCCCCCCTTCCTGTG
GATGGGCTACGAGCTGCACCCCGACAAGTGGACCGTGCAGCCCATCCAGCTGCCCGAGAAGGACTCCTGGACCGTGAACGAC
ATCCAGAAGCTGGTGGGCAAGCTGAACTGGGCCTCCCAGATCTACCCCGGCATCAAGGTGCGCCAGCTGTGCAAGCTGCTGC
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AGCAGCTGACCGAGGCCGTGCAGAAGATCGCCCAGGAGTCCATCGTGATCTGGGGCAAGACCCCCAAGTTCCGCCTGCCCAT
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CCCCTGGTGAAGCTGTGGTACCAGCTGGAGAAGGAGCCCATCGTGGGCGCCGAGACCTTCTACGTGGACGGCGCCGCCAACC
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GAAGACCGAGCTGCAGGCCATCAACCTGGCCCTGCAGGACTCCGGCTCCGAGGTGAACATCGTGACCGACTCCCAGTACGCC

CTGGGCATCATCCAGGCCCAGCCCGACAAGTCCGAGTCCGAGCTGGTGAACCAGATCATCGAGCAGCTGATCAAGAAGGAGA
AGGTGTACCTGTCCTGGGTGCCCGCCCACAAGGGCATCGGCGGCAACGAGCAGGTGGACAAGCTGGTGTCCTCCGGCATCCG
CAAGGTGCTGTTCCTGGACGGCATCGACAAGGCCCAGGAGGAGCACGAGAAGTACCACAACAACTGGCGCGCCATGGCCTCC
GACTTCAACCTGCCCCCCCGTGGTGGCCAAGGAGATCGTGGCCTCCTGCGACAAGTGCCAGCTGAAGGGCGAGGCCCTGCACG
GCCAGGTGGACTGCTCCCCCGGCATCTGGCAGCTGGACTGCACCCACCTGGAGGGCAAGGTGATCCTGGTGGCCGTGCACGT
GGCCTCCGGCTACATCGAGGCCGAGGTGATCCCCGCCGAGACCGGCCAGGAGACCGCCTACTTCCTGCTGAAGCTGGCCGGC
CGCTGGCCCGTGAAGGTGGTGCACACCGACAACGGCTCCAACTTCACCTCCGCCGCCGTGAAGGCCGCCTGCTGGTGGGCCG
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GAAGGGCGAGGGCGCCGTGGTGATCCAGGACAACTCCGACATCAAGGTGGTGCCCCGCCGCAAGGTGAAGATCATCAAGGAC
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1.125

82. 2003_CON_11_CPX pol.PEP

A

FFRENLAFQQGEAREFSPEQARANSPTSRELRVRGGDSPLPETGAEGEGAISFNFPQITLWQRPLVTIKVAGQLKEALLDTG
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KLKPGMDGPKVKQWPLTEEKIKALTEICTEMEKEGKISKIGPENPYNTPVFAIKKKDSTKWRKLVDFRELNKRTQDFWEVQL
GIPHPAGLKKKKSVTVLDVGDAYFSVPLDESFRKYTAFTIPSINNETPGIRYQYNVLPQGWKGSPAIFQSSMTKILEPFRTQ
NPEIVIYQYMDDLYVGSDLEIGQHREKVEELRKHLLKWGFTTPDKKHQKEPPFLWMGYELHPDKWTVQPIQLPDKECWTVND
IQKLVGKLNWASQIYPGIKVKQLCKLLRGTKALTDIVPLTAEAELELAENREILKEPVHGVYYDPSKDLIAEVQKQGLDQWT
YQIYQEPFKNLKTGKYAKRRTAHTNDVRQLAEVVQKISMESIVIWGKIPKFRLPIQRETWETWWTDYWQATWIPEWEFVNTP
PLVKLWYQLEKEPIIGAETFYVDGAANRETKLGKAGYVTDKGRQKVVTLTETTNQKTELEAIHLALQDSGLEVNIVTDSQYA
LGIIQAQPDKSESELVSQIIEQLIKKEKVYLSWVPAHKGIGGNEQVDKLVSSGIRKVLFLDGIDKAQEEHERYHSNWRAMAS
DFNLPPIVAKEIVASCDKCQLKGEAMHGQVDCSPGIWQLDCTHLEGKIILVAVHVASGYIEAEVIPAETGQETAYFILKLAG
RWPVKVIHTDNGSNFTSAAVKAACWWANIQQEFGIPYNPQSQGVVESMNKELKKIIGQVREQAEHLKTAVQMAVFIHNFKRK
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YGKQMAGDDCVAGRQDED$

2003_CON_11_CPX pol.OPT

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TTCTTCCGCGAGAACCTGGCCTTCCAGCAGGGCGAGGCCCGCGAGTTCTCCCCCGAGCAGGCCCGCGCCAACTCCCCCACCT
CCCGCGAGCTGCGCGTGCGCGGCGGCGACTCCCCCCTGCCCGAGACCGGCGCCGAGGGCGAGGGCGCCATCTCCTTCAACTT
CCCCCAGATCACCCTGTGGCAGCGCCCCCTGGTGACCATCAAGGTGGCCGGCCAGCTGAAGGAGGCCCTGCTGGACACCGGC
GCCGACGACACCGTGCTGGAGGAGATCGACCTGCCCGGCCGCTGGAAGCCCAAGATGATCGGCGGCATCGGCGGCTTCATCA
AGGTGCGCCAGTACGAGGAGATCATCATCGAGATCGAGGGCAAGAAGGCCATCGGCACCGTGCTGGTGGGCCCCACCCCCGT
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GCACCGAGATGGAGAAGGAGGGCAAGATCTCCAAGATCGGCCCCGAGAACCCCTACAACACCCCCGTGTTCGCCATCAAGAA
GAAGGACTCCACCAAGTGGCGCAAGCTGGTGGACTTCCGCGAGCTGAACAAGCGCACCCAGGACTTCTGGGAGGTGCAGCTG
GGCATCCCCCACCCCGCCGGCCTGAAGAAGAAGAAGTCCGTGACCGTGCTGGACGTGGGCGACGCCTACTTCTCCGTGCCCC
TGGACGAGTCCTTCCGCAAGTACACCGCCTTCACCATCCCCTCCATCAACAACGAGACCCCCGGCATCCGCTACCAGTACAA
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AACCCCGAGATCGTGATCTACCAGTACATGGACGACCTGTACGTGGGCTCCGACCTGGAGATCGGCCAGCACCGCGAGAAGG
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GATGGGCTACGAGCTGCACCCCGACAAGTGGACCGTGCAGCCCATCCAGCTGCCCGACAAGGAGTGCTGGACCGTGAACGAC
ATCCAGAAGCTGGTGGGCAAGCTGAACTGGGCCTCCCAGATCTACCCCGGCATCAAGGTGAAGCAGCTGTGCAAGCTGCTGC
GCGGCACCAAGGCCCTGACCGACATCGTGCCCCTGACCGCCGAGGCCGAGCTGGAGCTGGCCGAGAACCGCGAGATCCTGAA
GGAGCCCGTGCACGGCGTGTACTACGACCCCTCCAAGGACCTGATCGCCGAGGTGCAGAAGCAGGGCCTGGACCAGTGGACC
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GCCAGCTGGCCGAGGTGGTGCAGAAGATCTCCATGGAGTCCATCGTGATCTGGGGCAAGATCCCCAAGTTCCGCCTGCCCAT
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GAAGACCGAGCTGGAGGCCATCCACCTGGCCCTGCAGGACTCCGGCCTGGAGGTGAACATCGTGACCGACTCCCAGTACGCC
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GAAGGGCGAGGGCGCCGTGGTGATCCAGGACAACTCCGACATCAAGGTGGTGCCCCGCCGCAAGGCCAAGATCATCCGCGAC
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3.126

83. 2003_CON_12_BF pol.PEP

A

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VKLKPGMDGPKVKQWPLTEEKIKALTEICTEMEKEGKISKIGPENPYNTPVFAIKKKDSTKWRKLVDFRELNKRTQDFWEVQ
LGIPHPAGLKKKKSVTVLDVGDAYFSVPLDKDFRKYTAFTIPSVNNETPGIRYQYNVLPQGWKGSPAIFQSSMTKILEPFRK
QNPDIVIYQYMDDLYVGSDLEIGQHRTKIEELRQHLLRWGFTTPDKKHQKEPPFLWMGYELHPDKWTVQPIVLPEKDSWTVN
DIQKLVGKLNWASQIYPGIKVKQLCRLLRGTKALTEVIPLTKEAELELAENREILKEPVHGVYYDPSKDLIAEIQKQGQGQW
TYQIYQEPFKNLKTGKYARMRGAHTNDVKQLTEAVQKITTESIVIWGKTPKFRLPILKETWDTWWTEYWQATWIPEWEFVNT
PPLVKLWYQLETEPIAGAETFYVDGASNRETKKGKAGYVTDRGRQKAVSLTETTNQKAELHAIQLALQDSGSEVNIVTDSQY
ALGIIQAQPDKSESELVNQIIEQLIKKEKVYLSWVPAHKGIGGNEQVDKLVSAGIRKILFLDGIDKAQEEHEKYHNNWRAMA
SDFNLPPVVAKEIVASCDKCQLKGEAMHGQVDCSPGIWQLDCTHLEGKIILVAVHVASGYLEAEVIPAETGQETAYFILKLA
GRWPVKTIHTDNGPNFSSAAVKAACWWAGIQQEFGIPYNPQSQGVVESMNKELKKIIRQVRDQAEHLKTAVQMAVFIHNFKR
KGGIGGYSAGERIIDIISTDIQTRELQKQIIKIQNFRVYYRDSRDPVWKGPAKLLWKGEGAVVIQDNSEIKVVPRRKAKIIR
DYGKQMAGDDCVAGRQDED$

2003_CON_12_BF pol.OPT

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CCCGCGAGCTGTGGGTGCGCCGCGGCGACAACCCCCTGTCCGAGGCCGGCGCCGAGCGCCGCGGCACCGTGCCCTCCCTGTC
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GGCGCCGACGACACCGTGCTGGAGGACATCAACCTGCCCGGCAAGTGGAAGCCCAAGATGATCGGCGGCATCGGCGGCTTCA
TCAAGGTGAAGCAGTACGACAACATCCTGATCGAGATCTGCGGCCACAAGGCCATCGGCACCGTGCTGGTGGGCCCCACCCC
CGTGAACATCATCGGCCGCAACCTGCTGACCCAGCTGGGCTGCACCCTGAACTTCCCCATCTCCCCATCGAGACCGTGCCC
GTGAAGCTGAAGCCCGGCATGGACGGCCCCAAGGTGAAGCAGTGGCCCCTGACCGAGGAGAAGATCAAGGCCCTGACCGAGA
TCTGCACCGAGATGGAGAAGGAGGGCAAGATCTCCAAGATCGGCCCCGAGAACCCCTACAACACCCCCGTGTTCGCCATCAA
GAAGAAGGACTCCACCAAGTGGCGCAAGCTGGTGGACTTCCGCGAGCTGAACAAGCGCACCCAGGACTTCTGGGAGGTGCAG
CTGGGCATCCCCCACCCCGCCGGCCTGAAGAAGAAGAAGTCCGTGACCGTGCTGGACGTGGGCGACGCCTACTTCTCCGTGC
CCCTGGACAAGGACTTCCGCAAGTACACCGCCTTCACCATCCCCTCCGTGAACAACGAGACCCCCGGCATCCGCTACCAGTA
CAACGTGCTGCCCCAGGGCTGGAAGGGCTCCCCCGCCATCTTCCAGTCCTCCATGACCAAGATCCTGGAGCCCTTCCGCAAG
CAGAACCCCGACATCGTGATCTACCAGTACATGGACGACCTGTACGTGGGCTCCGACCTGGAGATCGGCCAGCACCGCACCA
AGATCGAGGAGCTGCGCCAGCACCTGCTGCGCTGGGGCTTCACCACCCCCGACAAGAAGCACCAGAAGGAGCCCCCCTTCCT
GTGGATGGGCTACGAGCTGCACCCCGACAAGTGGACCGTGCAGCCCATCGTGCTGCCCGAGAAGGACTCCTGGACCGTGAAC
GACATCCAGAAGCTGGTGGGCAAGCTGAACTGGGCCTCCCAGATCTACCCCGGCATCAAGGTGAAGCAGCTGTGCCGCCTGC
TGCGCGGCACCAAGGCCCTGACCGAGGTGATCCCCCTGACCAAGGAGGCCGAGCTGGAGCTGGCCGAGAACCGCGAGATCCT
GAAGGAGCCCGTGCACGGCGTGTACTACGACCCCTCCAAGGACCTGATCGCCGAGATCCAGAAGCAGGGCCAGGGCCAGTGG
ACCTACCAGATCTACCAGGAGCCCTTCAAGAACCTGAAGACCGGCAAGTACGCCCGCATGCGCGGCGCCCACACCAACGACG
TGAAGCAGCTGACCGAGGCCGTGCAGAAGATCACCACCGAGTCCATCGTGATCTGGGGCAAGACCCCCAAGTTCCGCCTGCC
CATCCTGAAGGAGACCTGGGACACCTGGTGGACCGAGTACTGGCAGGCCACCTGGATCCCCGAGTGGGAGTTCGTGAACACC
CCCCCCCTGGTGAAGCTGTGGTACCAGCTGGAGACCGAGCCCATCGCCGGCGCCGAGACCTTCTACGTGGACGGCGCCTCCA
ACCGCGAGACCAAGAAGGGCAAGGCCGGCTACGTGACCGACCGCGGCCGCCAGAAGGCCGTGTCCCTGACCGAGACCACCAA
CCAGAAGGCCGAGCTGCACGCCATCCAGCTGGCCCTGCAGGACTCCGGCTCCGAGGTGAACATCGTGACCGACTCCCAGTAC
GCCCTGGGCATCATCCAGGCCCAGCCCGACAAGTCCGAGTCCGAGCTGGTGAACCAGATCATCGAGCAGCTGATCAAGAAGG
AGAAGGTGTACCTGTCCTGGGTGCCCGCCCACAAGGGCATCGGCGGCAACGAGCAGGTGGACAAGCTGGTGTCCGCCGGCAT
CCGCAAGATCCTGTTCCTGGACGGCATCGACAAGGCCCAGGAGGAGCACGAGAAGTACCACAACAACTGGCGCGCCATGGCC
TCCGACTTCAACCTGCCCCCCGTGGTGGCCAAGGAGATCGTGGCCTCCTGCGACAAGTGCCAGCTGAAGGGCGAGGCCATGC
ACGGCCAGGTGGACTGCTCCCCCGGCATCTGGCAGCTGGACTGCACCCACCTGGAGGGCAAGATCATCCTGGTGGCCGTGCA
CGTGGCCTCCGGCTACCTGGAGGCCGAGGTGATCCCCGCCGAGACCGGCCAGGAGACCGCCTACTTCATCCTGAAGCTGGCC
GGCCGCTGGCCCGTGAAGACCATCCACACCGACAACGGCCCCAACTTCTCCTCCGCCGCCGTGAAGGCCGCCTGCTGGTGGG
CCGGCATCCAGCAGGAGTTCGGCATCCCCTACAACCCCCAGTCCCAGGGCGTGGTGGAGTCCATGAACAAGGAGCTGAAGAA
GATCATCCGCCAGGTGCGCGACCAGGCCGAGCACCTGAAGACCGCCGTGCAGATGGCCGTGTTCATCCACAACTTCAAGCGC
AAGGGCGGCATCGGCGGCTACTCCGCCGGCGAGCGCATCATCGACATCATCTCCACCGACATCCAGACCCGCGAGCTGCAGA

AGCAGATCATCAAGATCCAGAACTTCCGCGTGTACTACCGCGACTCCCGCGACCCCGTGTGGAAGGGCCCCGCCAAGCTGCT
GTGGAAGGGCGAGGGCGCCGTGGTGATCCAGGACAACTCCGAGATCAAGGTGGTGCCCCGCCGCAAGGCCAAGATCATCCGC
GACTACGGCAAGCAGATGGCCGGCGACGACTGCGTGGCCGGCCGCCAGGACGAGGACTAA

Fig. 127

A

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FFRENLAFQQGEAREFSPEQARANSPTRRELWVRRGDSPLPEARAEGKGDIPLSLPQITLWQRPLVTVRIGGQLIEALLDTG
ADDTVLEDINLPGKWKPKMIGGIGGFIKVRQYDQILIEICGKKAIGTVLVGPTPINIIGRNMLTQIGCTLNFPISPIETVPV
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GIPHPSGLKKKKSVTVLDVGDAYFSVPLDESFRKYTAFTIPSTNNETPGIRYQYNVLPQGWKGSPAIFQSSMTKILEPFRIK
NPEIVIYQYMDDLYVGSDLEIGQHRAKIEELRKHLLSWGFTTPDKKHQKEPPFLWMGYELHPDKWTVQPIQLPDKESWTVND
IQKLVGKLNWASQIYPGIKVKQLCKLLRGAKALTDIVPLTAEAELELAENREILKEPVHGVYYEPSKELIAEVQKQGLDQWT
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PLVKLWYRLETEPIAGAETYYVDGAANRETKLGKAGYVTDKGKQKIITLTETTNQKAELQAIHIALQDSGSEVNIVTDSQYA
LGIIQAQPDRSESEVVNQIIEQLIKKEKVYLSWVPAHKGIGGNEQVDKLVSSGIRKVLFLDGIDKAQEEHEKYHSNWRAMAS
DFNLPPVVAKEIVASCDKCQLKGEAMHGQVDCSPGIWQLDCTHLEGKIILVAVHVASGYIEAEVIPAETGQETAYFILKLAG
RWPVKIIHTDNGSNFTSAAVKAACWWANITQEFGIPYNPQSQGVVESMNKELKKIIGQVRDQAEHLKTAVQMAVFIHNFKRK
GGIGGYSAGERIIDIIASDIQTKELQKQITKIQNFRVYFRDSRDPIWKGPAKLLWKGEGAVVIQDNNEIKVVPRRKAKIIRD
YGKQMAGDDCVAGRQDED$

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B
TTCTTCCGCGAGAACCTGGCCTTCCAGCAGGGCGAGGCCCGCGAGTTCTCCCCCGAGCAGGCCCGCGCCAACTCCCCCACCC
GCCGCGAGCTGTGGGTGCGCCGCGGCGACTCCCCCCTGCCCGAGGCCCGCGCCGAGGGCAAGGGCGACATCCCCCTGTCCCT
GCCCCAGATCACCCTGTGGCAGCGCCCCCTGGTGACCGTGCGCATCGGCGGCCAGCTGATCGAGGCCCTGCTGGACACCGGC
GCCGACGACACCGTGCTGGAGGACATCAACCTGCCCGGCAAGTGGAAGCCCAAGATGATCGGCGGCATCGGCGGCTTCATCA
AGGTGCGCCAGTACGACCAGATCCTGATCGAGATCTGCGGCAAGAAGGCCATCGGCACCGTGCTGGTGGGCCCCACCCCCAT
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AAGCTGAAGCCCGGCATGGACGGCCCCAAGGTGAAGCAGTGGCCCCTGACCGAGGAGAAGATCAAGGCCCTGACCGACATCT
GCACCGAGATGGAGCGCGAGGGCAAGATCTCCAAGATCGGCCCCGAGAACCCCTACAACACCCCCATCTTCGCCATCAAGAA
GAAGGACTCCACCAAGTGGCGCAAGCTGGTGGACTTCCGCGAGCTGAACAAGCGCACCCAGGACTTCTGGGAGGTGCAGCTG
GGCATCCCCCACCCCTCCGGCCTGAAGAAGAAGAAGTCCGTGACCGTGCTGGACGTGGGCGACGCCTACTTCTCCGTGCCCC
TGGACGAGTCCTTCCGCAAGTACACCGCCTTCACCATCCCCTCCACCAACAACGAGACCCCCGGCATCCGCTACCAGTACAA
CGTGCTGCCCCAGGGCTGGAAGGGCTCCCCCGCCATCTTCCAGTCCTCCATGACCAAGATCCTGGAGCCCTTCCGCATCAAG
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TCGAGGAGCTGCGCAAGCACCTGCTGTCCTGGGGCTTCACCACCCCCGACAAGAAGCACCAGAAGGAGCCCCCCTTCCTGTG
GATGGGCTACGAGCTGCACCCCGACAAGTGGACCGTGCAGCCCATCCAGCTGCCCGACAAGGAGTCCTGGACCGTGAACGAC
ATCCAGAAGCTGGTGGGCAAGCTGAACTGGGCCTCCCAGATCTACCCCGGCATCAAGGTGAAGCAGCTGTGCAAGCTGCTGC
GCGGCGCCAAGGCCCTGACCGACATCGTGCCCCTGACCGCCGAGGCCGAGCTGGAGCTGGCCGAGAACCGCGAGATCCTGAA
GGAGCCCGTGCACGGCGTGTACTACGAGCCCTCCAAGGAGCTGATCGCCGAGGTGCAGAAGCAGGGCCTGGACCAGTGGACC
TACCAGATCTACCAGGAGCCCTACAAGAACCTGAAGACCGGCAAGTACGCCAAGCGCGGCTCCGCCCACACCAACGACGTGA
AGCAGCTGACCGAGGTGGTGCAGAAGATCGCCACCGAGTCCATCGTGATCTGGGGCAAGACCCCCAAGTTCAAGCTGCCCAT
CCGCAAGGAGACCTGGGAGGTGTGGTGGACCGAGTACTGGCAGGCCACCTGGATCCCCGACTGGGAGTTCGTGAACACCCCC
CCCCTGGTGAAGCTGTGGTACCGCCTGGAGACCGAGCCCATCGCCGGCGCCGAGACCTACTACGTGGACGGCGCCGCCAACC
GCGAGACCAAGCTGGGCAAGGCCGGCTACGTGACCGACAAGGGCAAGCAGAAGATCATCACCCTGACCGAGACCACCAACCA
GAAGGCCGAGCTGCAGGCCATCCACATCGCCCTGCAGGACTCCGGCTCCGAGGTGAACATCGTGACCGACTCCCAGTACGCC
CTGGGCATCATCCAGGCCCAGCCCGACCGCTCCGAGTCCGAGGTGGTGAACCAGATCATCGAGCAGCTGATCAAGAAGGAGA
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GACTTCAACCTGCCCCCCGTGGTGGCCAAGGAGATCGTGGCCTCCTGCGACAAGTGCCAGCTGAAGGGCGAGGCCATGCACG
GCCAGGTGGACTGCTCCCCCGGCATCTGGCAGCTGGACTGCACCCACCTGGAGGGCAAGATCATCCTGGTGGCCGTGCACGT
GGCCTCCGGCTACATCGAGGCCGAGGTGATCCCCGCCGAGACCGGCCAGGAGACCGCCTACTTCATCCTGAAGCTGGCCGGC
CGCTGGCCCGTGAAGATCATCCACACCGACAACGGCTCCAACTTCACCTCCGCCGCCGTGAAGGCCGCCTGCTGGTGGGCCA
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AGATCACCAAGATCCAGAACTTCCGCGTGTACTTCCGCGACTCCCGCGACCCCATCTGGAAGGGCCCCGCCAAGCTGCTGTG
GAAGGGCGAGGGCGCCGTGGTGATCCAGGACAACAACGAGATCAAGGTGGTGCCCCGCCGCAAGGCCAAGATCATCCGCGAC
TACGGCAAGCAGATGGCCGGCGACGACTGCGTGGCCGGCCGCCAGGACGAGGACTAA

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